

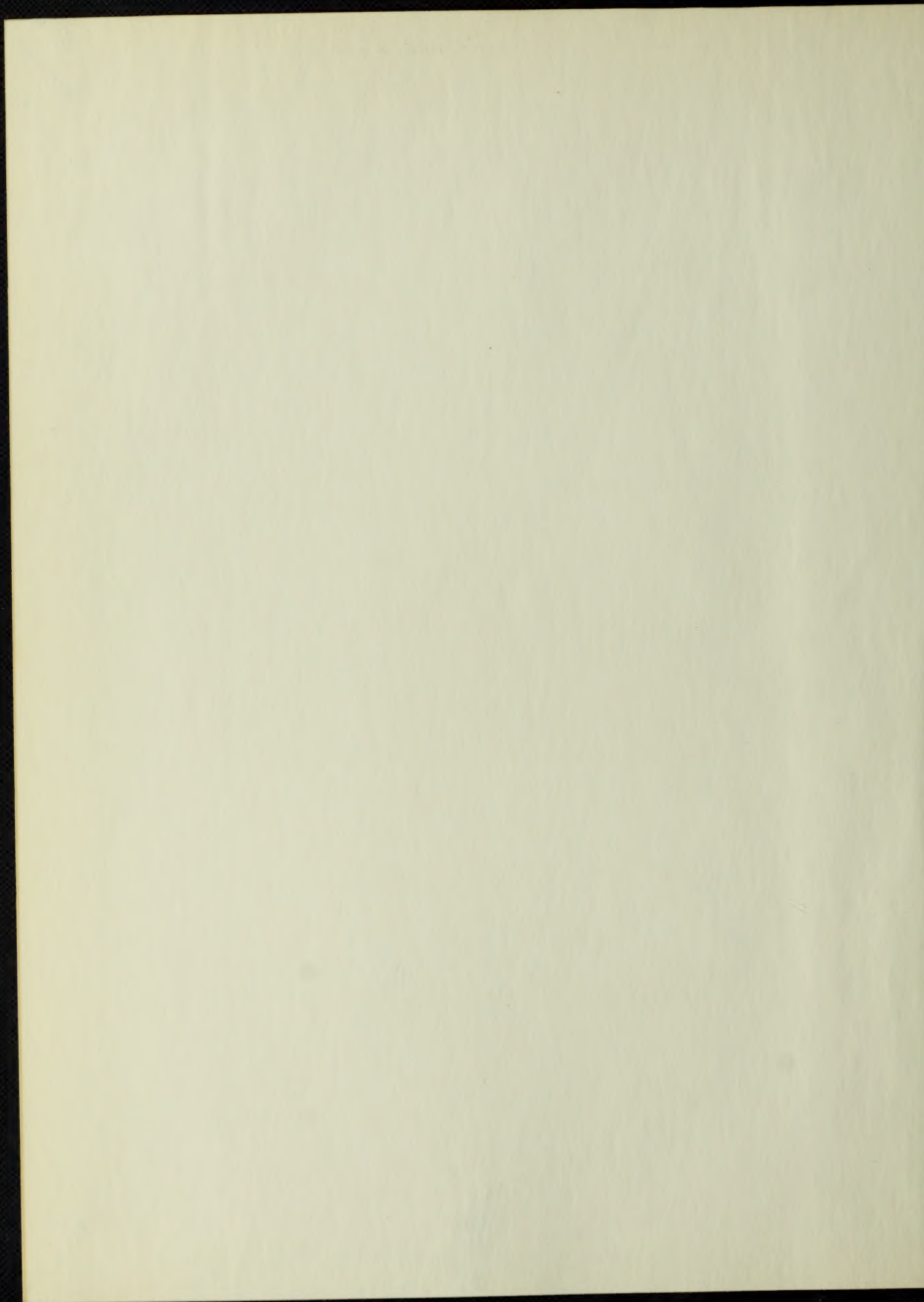
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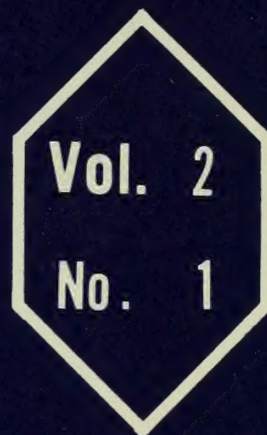
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CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE Public Health Service



CARCINOGENESIS ABSTRACTS

Volume 2, Number 1
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt(s).	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

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REVIEW

4-1 MEDICOLEGAL CONSIDERATIONS OF OCCUPATIONAL CANCERS. (Ger.) Hueper, W. C. (NCI, Bethesda). Pp. 1-122 in Beiträge zur Krebsforschung, Vol. 9. (Contributions to Cancer Research, Vol. 9), Leipzig, Theodore Steinkopff, 1964.

translation of "Medicolegal Considerations of Occupational Cancers" which appeared in Lawyers' Medical Cyclopedia (Frankel, C. J., Ed.). Indianapolis, Indiana, The Allen Smith Co., Vol. 1960, pp. 558-663. (Approx. 720 references)

4-2 INFLUENCE OF INFECTION AND TOXINS FROM BACTERIA, FUNGI AND PARASITES ON THE EVOLUTION OF TUMORAL PROCESSES. (Fr.) Lavina, A. Presse Med. 72(8):451-456, 1964.

review of instances in which concurrent or previous bacterial infections or the inj. of different biological products derived from living organisms significantly altered the course of neoplastic disease or the incidence of metastases. The author concludes that there are viruses not only capable of inhibiting the growth of certain tumors but also capable of inducing tumor regression; and a potentially very large number of bacterial, fungal, or parasitic derivatives with significant antitumor effects. He also concludes that cancerous cells are much more susceptible than normal cells to both groups of potential agents. (3 references)

-3 CAN LEUKEMIA BE CONSIDERED AN INFECTIOUS DISEASE? (Fr.) Lépine, P. (Dept. Virol., Pasteur Inst., Paris). Nouv. Rev. Franc. Hemat. 3(6):817-830, 1963.

a general review of virus-induced experimental leukemias, the author concludes that mouse leukemias are probably caused, in most cases, by a virus of the Furth-Gross type, but that other viruses cannot be eliminated. Such virus-infections may be masked, and the virus, attached to the genome, may be transmitted to succeeding generations, remaining latent until it is activated by a precipitating factor such as exposure to X-ray. In discussion, Lépine commented on Latarjet's suggestion that attachment of the virus to the genome need not necessarily be stimulated; a fraction of the genome which had been damaged by the virus might be transmitted in damaged form after the virus had disappeared, interacting with a cellular genome in some later generation to create a malignant mutation. (See also CRA 1(8):#1422, 1963.) (43 references)

-4 HISTOCHEMISTRY OF SOME ASPECTS OF PROSTATE PATHOLOGY. (E.) Brandes, D. (Johns Hopkins U. Sch. Med., Baltimore, Md.) and H. Bourne. Nat. Cancer Inst. Monogr. (12): 41, 1963.

A review of the histological and cytological changes in distribution of various compounds found in the prostate under normal, carcinomatous, and other conditions. No detectable change could be found in reactions of human normal and adenomatous prostates when subject to PAS, Sudan Black, acid and alkaline phosphatases, and 5-nucleotidase reactions. Previously reported decreases in the esterase reaction in prostatic adenomas and carcinomas have not been confirmed by improved histochemical technics. In carcinomatous material there has been noted reduction in the PAS reaction and increase of sudanophil fat in some epithelial cells. The role of estrogen phosphates is reviewed. (20 references)

64-5 RADIOACTIVITY, ISOTOPES AND CANCER. (Por.) Placco, R. A. (Dept. Med., Adolfo Lutz Inst., Sao Paulo, Brazil). Hospital (Rio) 64(6):1451-1458, 1963.

In a review centering on the radioactive isotopes, the author warned of their possible carcinogenic effects and of those of X-ray or exposure to other sources of irradiation. (No references)

64-6 ELEMENTS FAVORING AN INCREASED INCIDENCE OF PRIMARY BRONCHOPULMONARY CARCINOMA. (It.) Bonini, A. (1st Div. Med., Riuniti Hosp., Trieste, Italy), V. Bruno and L. Tenze. Rass. Clin. Ter. 57(4):272-285, 1963.

In a general review of published statistics on the incidence of primary bronchogenic carcinoma, the authors conclude that the smoke of tobacco, in addition to its own carcinogenic effect, may bring about histologic changes which favor the development of lung cancer. They also believe atmospheric pollution may have a cocarcinogenic effect. (59 references)

64-7 ETIOLOGY AND PATHOGENESIS OF CANCER. (Ger.) Schümmelfeder, N. (Inst. Path., U. Cologne, Germany) and J. Gimmy. Munch. Med. Wschr. 106(1):1-11, 1964.

A general review emphasizes the role of genetic changes in carcinogenesis and also includes discussions of physical and viral agents as well as organic and inorganic carcinogens. (11 references)

64-8 CARCINOGENESIS. RECENT TRENDS. (E.) Chawla, L. S. (Dept. Path., Coll. Med., Amritsar, India) and T. D. Sharma. Licentiate 13(4):103-108, 1963.

A brief, very general review of classes of carcinogens and theories of carcinogenesis. The type of agent, susceptibility and the time element are considered the main factors; the appearance

of cancer is directly related to their strength and duration. (No references)

- 64-9 WHO EXPERTS ON THE PREVENTION OF CANCER. (E.) Epidemiological Notes. Med. Officer 109(3):39-40, 1964.

The WHO Expert Committee on the Prevention of Cancer, at a recent meeting in Geneva, reported on the following causes of cancer: industrial hazards; air pollution; ionizing radiations; food additives; cosmetics and household products; smoking; medicaments (including plastic surgical devices); betel, nass and tobacco chewing; alcohol; food and water; sex hygiene; lactation; and sunshine. It is stated that cancer prevention should start with the central government of a country and this should be followed by steps to integrate activities on an international level. For a well defined carcinogenic substance, it is suggested that legislative action should help to eliminate it from industry. (No references)

- 64-10 DISCUSSION ON CELL DESTRUCTION AND POPULATION DYNAMICS IN EXPERIMENTAL SKIN CARCINOGENESIS IN MICE. (E.) Iversen, O. H. (Inst. Gen. Exp. Path., U. Oslo, Norway). Progr. Exp. Tumor Res. 4:169-206, 1964.

In a discussion and review on cell destruction and population dynamics in hairless mice, the effects of a single application of 20-methyl-cholanthrene (MC; 0.005 ml of 1% soln.) in benzene on formazan deposition (see CRA 1(2):#243, 1963), oxygen consumption, cell proliferation (see CRA 1(6):#1050, 1963) and cell counts are presented. The mathematical calculations for these studies were also included and it was concluded that cell damage is a direct carcinogen effect, while cell proliferation leading to hyperplasia is a secondary effect. Repeated applications (4) of MC (no details) increased the number of labeled cells (after prior H³-thymidine inj.) and the mitotic count during the 11 days after each application, while repeated MC applications decreased the rate of formazan deposition. (See also CRA 2(1):#61, 1964.) (42 references)

- 64-11 CYTOCHEMICAL ASPECTS OF EXPERIMENTAL LEUKEMIA. (E.) Thorell, B. (Dept. Path., Karolinska Inst., Stockholm, Sweden). Internat. Rev. Exp. Pathol. 2:47-66, 1963.

A review of the cytogenesis of the virus-induced leukemia cell in relation to normal hematopoiesis, the biochemistry of chicken leukemia virus and the relationships between virus and target cell is presented, using mainly the author's own experiments with physico-optical and chemical methods. The cytotopographic, cytogenetic and metabolic relationship between virus and target cells is also discussed. (For related studies,

see CRA 1(4):#612; ibid., (7):#1212, 1963.) (53 references)

- 64-12 BIOLOGICAL EFFECTS OF IONIZING RADIATIONS. (E.) Upton, A. C. (Oak Ridge Natl. Lab., Tenn.). Internat. Rev. Exp. Pathol. 2:199-240, 1963.

A survey of those aspects of the subject which are of major relevance to experimental pathology. It was concluded that in general, gene mutation, chromosome breakage, and inhibition of reproduction are among the most radiosensitive responses of the cell; undifferentiated stem cells are among the most sensitive since only small radiation doses are needed to inhibit such dividing cells, rather than killing them outright. Cell killing need not be linked to mitotic disturbance as is indicated by the high radiosensitivity of certain nondividing mammalian cells such as small lymphocytes, oocytes, and neuroblasts. Late somatic effects of radiation, resembling lesions associated with senescence (although their relation, if any, to these are obscure) include neoplasia, nephrosclerosis, vascular degeneration, and other degenerative changes. In the induction of certain murine leukemias, radiation appeared to activate a latent leukemogenic virus. It was indicated that there is growing evidence for the existence of homeostatic or reparative mechanisms (apparently dependent on cellular metabolism) operating within the cell to counteract radiation effects. (Approx. 200 references)

- 64-13 IS CANCER INDUCED BY A VIRUS? (Fr.) Lutte Cancer 40(142):16-18, 1963.

A brief discussion is presented of work by L. A. Zilber (see CRA 1(7):#1213, 1963). (No references)

- 64-14 THE RELATION OF IMMUNITY TO CANCER ETIOLOGY. (E.) Hadley, H. G. (Res. Found., Inc., Washington, D. C.). Sem. Med. (B. Air.) 123(23):889-891, 1963.

A briefer presentation of the review abstracted as CRA 1(5):#783, 1963 with chief emphasis on the immunologic aspects of cancer etiology. (11 references)

- 64-15 RELATION BETWEEN IMMUNITY TO BACTERIA AND NEOPLASIA. (Sp.) Hadley, H. G. (Hadley Mem. Hosp., Washington 24, D. C.). Rev. Confed. Med. Panamericana 10(2):87-88, 1963.

See CRA 1(5):#783, 1963. (8 references)

- 64-16 THE INCREASING MENACE OF BRONCHOGENIC CANCER. (E.) Ochsner, A. (Alton

chsner Clin., New Orleans, La.). New Physician 3(2):29-36, 1964.

An extensive report and review on the incidence of bronchogenic cancer, the incidence of smoking among physicians and teen-agers, the amount of cigarette consumption today and the effects of filters and smog are presented. (35 references)

4-17 THE HAZARD OF BRONCHOGENIC CARCINOMA AND ITS PREVENTION. (E.) Ochsner, A. Dept. Surg., Ochsner Clin., New Orleans, La.). Milit. Med. 128(12):1167-1172, 1963.

See the preceding abstract (CRA 2(1):#16, 1964). 28 references)

4-18 IMMUNITY REACTIONS TO CANCER. (E.) Editorial. Brit. Med. J. 1:2-4, 1964.

In a discussion of immunity reactions to cancer, Murphy noted that the body's resistance to transplanted and spontaneous tumors was mediated by the lymphoid tissue and a local lymphocytic reaction occurred in animals resistant to grafted tumors. Suppression of lymphoid tissue by X-irradiation at high dosages aided tumor growth, while X-irradiation at low dosages enhanced lymphoid tissue activity and thereby inhibited tumor growth. S. de Carvalho's attempt at passive immunization by the inj. of a special 90-95% pure serum γ -globulin (obtained by inj. horses and donkeys with human "cancer" antigens from which normal tissue specific antigens had been adsorbed by an appropriate antiserum) resulted in some clinical benefit in 31 pts. suffering from various types of leukemia and cancer. Other methods of increasing body immunity to tumors are described. When Haddow and P. Alexander attempted to reinforce the antigenicity of the benzpyrene-induced rat sarcoma by reimplantation of pieces of lethally irradiated tumor, the procedure in itself was not effective, but the sensitivity to chemotherapy was increased. (43 references)

64-19 TOLERANCE OF IRON THERAPY WITH CONSIDERATION OF CARCINOGENIC EFFECT OF THE DEXTRAN-IRON COMPLEX. (Ger.) Thederling, F. (Dept. Int. Med., Pius Hosp., Oldenburg, Germany). Med. Welt (6):277-282, 1964.

Various forms of iron therapy (for deficiencies) are discussed, and a review of literature emphasizing the low probability of carcinogenic action of the dextran-iron complex (Myofer, Imferon) is presented. So far only local carcinogenic effects were found and only after s.c. inj. in rats and mice (but not after i.m. inj. and not in hamsters, guinea pigs, or rabbits). In humans, a total of 40 million i.m. inj. in 3 million pts. within about 10 yr. has caused no local primary sarcomas to date. Only 1 case was found in the literature where a pt. with stage II uterine carcinoma developed a metastasis at the site of i.m. inj. of a total of 2500 mg of Imferon. This phenomenon was ascribed mainly to the trauma of inj. Examples of trauma due to penicillin inj., inflammation, or other injury as factors promoting distant metastasizing of an already primary cancer are mentioned. (No references)

64-20 THE SEPARATION AND ANALYSIS OF POLYNUCLEAR AROMATIC HYDROCARBONS PRESENT IN THE HUMAN ENVIRONMENT. II. (E.) Sawicki, E. (Robert A. Taft Sanitary Engineering Ctr., Cincinnati, Ohio). Chem. Anal. 53(2):56-62, 1964.

The author reviews 3 methods (paper chromatography, thin-layer chromatography, gas chromatography) for separating and analyzing polynuclear aromatic hydrocarbons present in the human environment. Several tables present Rf values of a number of compounds upon analysis by paper and thin-layer chromatography; similarly relative retention times are given of compounds analyzed by gas chromatography. (55 references)

See also abstract nos.: 21,126

PHYSICAL CARCINOGENESIS

- 64-21 MALIGNANT DISORDERS AND SMALL DOSES OF IONIZING RADIATIONS. (Fr.) Delpla, M. *J. Radiol. Electr.* 44(12):157-165, 1963.

In a review (23 references) of the carcinogenic effects of both total and local irradiation, the author concludes that we know absolutely nothing, to date, concerning the possible carcinogenic effects of small doses of X-ray or other ionizing radiations, and that the subject has yet to be investigated under conditions which would permit drawing conclusions having any statistical reliability.

- 64-22 ELECTRON MICROSCOPIC FINDINGS IN FIBRO-ADENOMA IN THE RAT INDUCED BY WHOLE BODY X-IRRADIATION. (Jap., Abstract) Matsuoka, K. (Dept. Path., Nagasaki U. Sch. Med., Japan), T. Tanida, T. Uga, E. Funakoshi and G. Matsukuma. *Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.)* 52:225-227, 1963.

Among 1550 female Wistar rats admin. general X-irradiation (5 r to 500 r; no details) from age 5 days to 4 mo., 12 developed fibroadenoma of the breast. When these were subjected to electron microscopic study, no marked differences were noted compared to 2 fibroadenomas that developed spontaneously in a control group.

- 64-23 PROTRACTED EFFECTS OF REPEATED DOSES OF X-RAY IRRADIATION IN RATS. (E.) Berdjis, C. C. (U. S. Army Med. Unit, Fort Detrick, Md.). *Exp. Molec. Path.* 2(2):157-172, 1963.

Sprague-Dawley rats (age 90-150 days) were irradiated at 4 wk. intervals during a 6-mo. period with 3 x 350 r (total body), 1000 r (chest), 900 r (both kidneys), and 500 r (total body). The 37/52 survivors in the treated group and the 36/40 survivors among controls were autopsied at death or sacrificed at 24-27 mo. of age (each group contained 19 males). There were a total of 172 tumors in irradiated rats (4.6/animal); there were 27 in controls (1.3/animal). Repeated X-irradiation appeared to be highly carcinogenic with a selective effect upon the endocrine organs and the related governing systems: treated rats showed the following tumors--pituitary 7, parathyroid 7, pancreas 8, thyroid 9, adrenal 8, testis 11, and ovary 10 (total 60). In controls, these tumors numbered, resp., 3, 0, 2, 3, 1, 2, and 2 (total 13). This predilection is considered to be of the greatest interest in correlating the "mutagenic theory of cancer" and "hormonal imbalance" in radiation research. A pluriglandular syndrome consisting of multiple endocrine adenomas, intimately related to gastrointestinal and genitourinary disorders as in man, was encountered in several animals.

- 64-24 RADIOGRAPHIC CHANGES FOLLOWING THE ADMINISTRATION OF BONE-SEEKING RADIO-NUCLIDES. (E.) Fabrikant, J. I. (Dept. Phys., Inst. Cancer Res., Belmont, Sutton, Surrey, England) and C. L. D. Smith. *Brit. J. Radiol.* 37(433):53-62, 1964.

Radionuclides (α -emitting Pu²³⁹ and Am²⁴¹ and β -emitting P³²) were admin. to male rats of the Marshall and August strains or F₁ male hybrids from parents of these strains either in a single inj. or inj. repeated after 2, 4, 6 and 8 wk. After single and repeated i.p. doses of P³² (3.0 μ C/g total activity in either case) to young rats (age 6-8 wk.) there were, resp., 7/31 and 9/15 tumor-bearing animals. Early radiographic changes were apparent after 6 and 3 mo., resp., while tumors appeared after an av. period of 8 and 5 mo. After i.v. admin. of Pu²³⁹, single and repeated doses to young rats (total activity 2.95 and 3.0 μ C/kg, resp.) and single doses to old rat (7 mo., total activity 2.95 μ C/kg), tumor-bearing animals numbered, resp., 13/25, 14/25 and 4/15; tumors numbered 25, 25 and 5. Tumors were apparent after an av. period of 15, 10 and 15 mo., resp. After single inj. of Am²⁴¹ at 2 dose levels, total activity 2.5 and 5.8 μ C/kg, there were, resp., 4/32 and 4/30 tumor-bearing animals, each group with 5 tumors. Early changes were apparent at about 12 mo. and tumors by 15.5-22 mo. and <12-14 mo., resp. Among the lesions observed were failure of longitudinal bone growth, abnormal bone molding, pathological fractures, and the production of sclerosing, lytic, and mixed forms of osteosarcoma. (See also CRA 1(8):#1448, 1963.)

- 64-25 BONE SARCOMAS FOLLOWING RADIATION THERAPY. (E.) Phillips, T. L. (Dept. Radiol., U. California Sch. Med., San Francisco) and G. E. Sheline. *Radiology* 81(6):992-996, 1963.

Among approx. 6000 pts. treated at the Radiation Therapy Dept., only 2 (0.03%) of those treated or 0.1% of 2300 5-year survivors developed osteogenic sarcoma in irradiated bone. The case histories presented were in pts. treated for carcinoma of the breast and cervix; both occurred in previously normal bone and the latent periods were 11 and 5 yr. It is concluded that the complication of bone sarcoma is so rare (only 30 cases reported in normal bone) that it constitutes no contraindication to the use of radiation therapy for malignant disease. Since 50 cases of bone sarcoma following irradiation of benign bone tumors have been reported it is deemed advisable to avoid irradiation of these lesions when they are readily amenable to operative procedure without high morbidity. (See also CRA 1(2):#188, 1963.)

- 64-26 BONE TUMOUR PRODUCTION IN MICE BY STRONTIUM-90: FURTHER EXPERIMENTAL

SUPPORT FOR A TWO-EVENT HYPOTHESIS. (E.) Mole, R. H. (Med. Res. Council Radiobiol. Res. Unit, Harwell, Didcot, Berks, England). Brit. J. Cancer 17(3):524-531, 1963.

The data of various workers (L. M. van Putten and M. J. de Vries, 1962; and L. M. van Putten, 1962) on bone tumor production by strontium-90 in mice were analyzed. In addition, unpublished information on time of death of each mouse and number of tumors carried was incorporated into the analysis. It was concluded that the rate of appearance of tumors with time after admin. is proportional to the square of the number of radioactive disintegrations within the skeleton in the time interval before the tumor is induced.

64-27 GENOME CHANGES IN ACQUIRED RESISTANCE TO RADIATION. (Ger.) Bhaskaran, S. (Inst. Radiol. Biol., Nucl. Res. Ctr., Karlsruhe, Germany) and W. Dittich. Strahlentherapie 22(2):270-278, 1963.

Radiation resistant lines of Ehrlich ascites tumor were developed in three hyperdiploid lines (SOELD 1, SOELD 2) and 1 hypertetraploid line (ET) by serial radiation (1000 r) under aerobic conditions; this resistance persisted after 100 animal passages. The acquired radio-resistance of the tumor, following a single irradiation, is expressed in part by an increase in malignancy; e.g., 13 days after transplantation of 2×10^7 radioresistant cells of line SOELD 1 into 8 groups of 24 mice each only 0-14 (av. 6.25) survived compared to 11-23 (av. 17) controls which received non-irradiated SOELD 1 cells. Some morphological chromosome changes were noted in the irradiated tumor lines, and the modal chromosome number was increased by 2.

64-28 PERITONEAL TUMOURS IN ASBESTOSIS. (E.) Enticknap, J. B. (East Ham Mem. Hosp., Essex, England) and W. J. Smither. Brit. J. Industr. Med. 21(1):20-31, 1964.

Eleven cases (8 male, 3 female) of diffuse abdominal tumors were reported from 1958-1963 which were involved in contact with 3 grades of commercial asbestos for periods (not always consecutive) ranging from 10 mo. to 32 yr. Age at death ranged from 38-78 yr. with one pt. (age 46) still alive 26 yr. after first exposure. Survival time after the first exposure was 20-46 yr.; survival

time after onset of symptoms was 2-19 mo. with one pt. alive after 10 mo. The tumor material consisted mostly of irregular fibrous tissue in which a variable number of clefts had formed. The cases were characterized by minimal fibrosis in the lungs and no pt. was completely disabled by pulmonary fibrosis.

64-29 RADIOGENIC LUNG CANCER. (E.) Cember, H. (Kettering Lab., U. Cincinnati Coll. Med., Ohio). Progr. Exp. Tumor Res. 4:251-303, 1964.

Rats subjected to aerosol inhalation of $\text{BaS}^{35}\text{O}_4$ and $\text{Na}_2\text{S}^{35}\text{O}_4$ showed no lung changes from acute doses (single 2-hour exposure), while in chronically exposed animals (10 two-hour exposures at biweekly intervals) reticulum cell sarcoma of the lung developed in 1/26 rats from the $\text{Na}_2\text{S}^{35}\text{O}_4$ group and in 2/28 rats from and $\text{BaS}^{35}\text{O}_4$ group, the latter group also showing nonmalignant lung fibroadenomas in 2 rats. Single intratracheal (IT) inj. of 26 μg of $\text{BaS}^{35}\text{O}_4$ particulates suspended in 0.5 ml isotonic saline in rats showed neither lung cancer nor any other suggestive lesions. Multiple IT inj. in rats of $\text{BaS}^{35}\text{O}_4$ (375 $\mu\text{C}/\text{wk.} \times 10$) revealed 2/16 with extensive squamous cell lung carcinoma, 2/16 with extensive squamous cell lung metaplasia and 1/16 with a lesion diagnosed as either premalignant dysplasia or carcinoma *in situ*. When external X-irradiation, at treatment levels of 5,000, 10,000, and 15,000 rads, was admin. to rats in fractionated doses during a 1-week period, incidence of lymphomas was 2, 1 and 1, resp. After implantation of radioactive beads ($\text{Sr}^{90}\text{-Y}^{90}$ as $\text{Sr}^{90}\text{CO}_3$ fused with ground soft glass) in the lungs of 23 rats, 4 bronchogenic squamous cell carcinomas, 2 lymphosarcomas and 1 lymphoma were found. After IT inj. of 0.15 ml of an aqueous soln. of 30 μg $\text{Ce}^{144}\text{F}_3$ as 1 micron particulates at Ce^{144} dose levels of 50, 25, 15 and 5 μC , incidence of bronchogenic squamous cell carcinomas was 4/15, 7/28, 1/23 and 1/27, resp.; there was also widespread squamous metaplasia of the bronchial and alveolar epithelium in all rats. For a low level study of $\text{Ce}^{144}\text{F}_3$ carcinogenesis, see CRA 1(8):#1445, 1963. In rats treated by IT inj. of $\text{Ce}^{144}\text{Cl}_3$ at dose levels of 10, 15 and 30 μC , a total of 67 primary lung cancers were observed among the 150 2-month survivors including 47 squamous cell carcinomas, 7 alveolar cell carcinomas, 4 adenocarcinomas and 4 lymphomas. A review is also presented of other work on lung cancer induced by radioactive substances (76 references).

See also abstract nos.: 5,12,44,59,70

CHEMICAL CARCINOGENESIS

- 64-30 CHEMICAL INDUCTION OF MAMMARY CANCER IN GERM-FREE RATS. (E.) Pollard, M. (Lobund Lab., U. Notre Dame, Ind.). *Nature* (London) 200:1289-1291, 1963.

Thirty-eight female Wistar, Fischer and Sprague-Dawley rats at 50-60 days old, both germfree and conventional counterparts, were fed a single dose of 9,10-dimethyl-1,2-benzanthracene (20 ml in 1 ml of sesame oil) by stomach tube. The germfree animals were kept in a germfree state thereafter. Mammary tumors (1-8/animal) developed in 9/9 germfree Sprague-Dawley rats (av. latent period: 82 days) and in 16/18 of the conventional counterparts at av. of 103 days with essentially the same distribution of tumors. Breast tumor was detected in 1/5 germfree Wistar rats after an av. of 111 days. All 15 germfree Fischer rats died in 15 days with no evidence of tumor formation. All 12 Wistar and 9 Fischer conventional rats survived but none developed tumors. All mammary tumors were solid, circumscribed adenocarcinomas. These findings support the concept that there are multiple initiators of the same cellular alterations, evoked by chemical, physical, or biological agents, leading to a neoplastic transformation. For earlier studies, see CRA 1(1):#59; *ibid.*, (6):#1100 and *ibid.*, (7):#1341, 1963.

- 64-31 ASCORBIC ACID PROTECTION AGAINST TOXICITY OF AN AZO DYE CARCINOGEN FOR *NEUROSPORA CRASSA*. (E.) Bobb, D. (Palo Alto Med. Res. Found., Cal.). *Biochim. Biophys. Acta* 78(4): 795-797, 1963.

This report deals with the ability of l-ascorbic acid to overcome the growth inhibition effect (manifested by prolonged lag phase) of 3'-methyl-4-monomethylaminoazobenzene (MeMAB) on 2 strains of *Neurospora crassa*. Wild-type strain STA proved relatively resistant, while riboflavin-deficient strain 51602 was the most sensitive to azo dye inhibition. At a given MeMAB conc., increasing amounts of the vitamin produced progressively greater protective effects (up to a molar ratio of vitamin/dye of about 100:1). Both d-isoascorbic acid and dehydroascorbic acid could replace the l-ascorbic acid; its protective effect, however, was nullified in presence of either cysteine or GSH [glutathione]. The significance of the present findings with respect to azo dye carcinogen induction of hepatomas in the rat is uncertain.

- 64-32 CARCINOGENIC POTENTIALS OF MEDICATIONS. THIRD SCIENTIFIC SESSION OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF TOXICITY OF MEDICATIONS. (LAUSANNE, JANUARY 10, 1964.) (Fr.) Editorial. *Med. Hyg. (Geneve)* 22(625):20, 1964.

A general review of some of the papers given at the conference. A. L. Walpole emphasized that carcinogenic activity was a function of many,

interacting factors (including route, duration and frequency of admin.), and that there was no direct or *a priori* relationship between toxicity and carcinogenic potential. J. Elis pointed out that the presence of antimetabolic, antitumor, contraceptive, mutagenic, teratogenic, cytostatic, or other effects could not be considered an indication or contraindication of possible carcinogenic activity as concerned any medication. G. Della Porta detailed the technical and other conditions necessary for meaningful experimental study of such possible effects, but cautioned against drawing any conclusions with respect to human pts. on the basis of such studies alone. M. Marois reviewed the possible carcinogenic effects of the estrogens, especially during menopause, in the presence of certain types of cervical, uterine or mammary tumors, or in the presence of hereditary familial predisposition to susceptibility. R. Truhaut discussed the role and responsibilities of public health authorities with respect to control of medications. Also discussed at some length was the need for establishing cooperative study groups for the investigation of new or suspected medications, similar to those which now exist for evaluating cancer chemotherapeutic agents.

- 64-33 TUMOR-ENHANCING ACTIVITY OF THE ACTIVE PRINCIPLES OF *CROTON TIGLIUM* L. (E.) Van Duuren, B. L. (Inst. Indust. Med., New York U. Med. Ctr., N.Y.), L. Orris and E. Arroyo. *Nature* (London) 200(Suppl.):1115-1116, 1963.

The promoting activity of various principles of *Croton tiglium* (described in an earlier paper) was tested after topical admin. in Swiss Millerton mice after initiation with 9,10-dimethyl-1,2-benzanthracene (DMBA; topical, 150 µg) applied 14 days previously. When compared to DMBA + whole croton seed extract, a croton resin and its subfraction, in which concentration of activity had been achieved, showed high incidences of papillomas. After 1 yr. 70% of surviving animals which had received DMBA + croton resin had squamous cell epidermoid carcinomas. Progressive purification of the biologically active mixture led to 2 components labeled A and C; both are powerful irritants. Two wk. after initiation with 300 µg DMBA, groups of 20 female mice received promoting compound A or C (each 5 µg in acetone 3x/wk.). After 8 wk. (cumulative promoter per animal, 120 µg) number of tumor-bearing animals was, resp., 2 and 17; after 14 wk., all animals survived and there were 15 and 20 tumor-bearers (cumulative promoter per animal, 210 µg). Tumors were not observed in appropriate control groups. It is stated that activity of compounds A and C is much higher than that reported for other tumor-enhancing agents such as phenol, the "Tweens" and "Spans". One yr. after initiation with 150 µg of DMBA, 11/18 survivors received topical application of croton resin (25 µg in

cetone, 3x/wk.). After 120 days 4 animals had papillomas and 2 squamous cell epidermoid carcinomas. In a parallel DMBA-only group there were no skin tumors.

4-34 ACCELERATION OF THE DEVELOPMENT OF LEUKEMIA AND INDUCTION OF TUMORS IN AKR MICE BY NEONATAL INJECTION OF 20-METHYLCHOLANTHRENE. (E.) Miyoshi, I. (Dept. Int. Med., Okayama U. Sch. Med., Japan). Acta Med. Okayama 7(1):51-61, 1963.

Neonatal inj. of 20-methylcholanthrene (0.5 mg in 0.1 ml, s.c.) accelerated the development of implanted lymphocytic leukemia in 2/4 surviving AKR mice. Latent period was 101 and 131 days, compared to 6 mo. or longer for the development of spontaneous leukemia in this strain. In addition there were 1 s.c. sarcomas in 3 mice and 136 multiple pulmonary adenomas (19-60 tumors/mouse) among all 4 mice. No lung adenomas were found in 11 control mice. It is suggested that the lungs of newborn mice of strain AKR may prove to be sensitive organs to evaluate the carcinogenicity of certain carcinogens.

4-35 EFFECT OF METHYLCHOLANTHRENE ON BRAIN OF DUCKS. (E.) Omer, S. (Andhra Med. Coll., India). Indian J. Med. Res. 51(6):997-1004, 1963.

No tumors were observed within 370 days after 20-methylcholanthrene (approx. 5 mg crystals compressed in a pellet) was implanted through a burr hole deep into the right cerebral hemisphere of 5 white Pekin ducks (3 wk.-6 mo. old). Neurological damage was observed in 3, acute necrotic liver lesions in 2. The pellet produced hemorrhage and necrosis in the brain tissue which was followed by a leukocytic and microglial response. Capsule of foreign body giant cells and reticulum formed about the pellet as early as the 7th day. A brief review of the literature on experimental and spontaneous brain tumors in animals and birds is given (31 references).

4-36 EFFECT OF 2-METHYL-1,2-bis-(3-PYRIDYL)-1-PROPANONE (METYRAPONE) ON THE PRODUCTION OF MAMMARY TUMOURS INDUCED IN RATS BY ORAL FEEDING WITH DIMETHYLBENZANTHRACENE. (E.) Helfenstein, J. E. (Path. Unit, Imperial Cancer Res. Fund, London, W.C.2) and S. Young. Nature (London) 200 (Suppl.):1113-1114, 1963.

The group of 220 Sprague-Dawley rats, age 54 days, was given 2-methyl-1,2-bis-(3-pyridyl)-1-propanone (Metyrapone, M; 40 mg in corn oil, s.c.) followed 2 hr. later by 9,10-dimethyl-1,2-benzanthracene (DMBA; 50 mg in corn oil, intragastrically); a similar group of 220 received only DMBA. When 20% were killed on day 3, adrenal necrosis was seen in 23/33 and 31/40, resp. During the first 3 mo., while fewer rats in the DMBA + M group developed

mammary tumors, this difference was not significant. By day 100 there were 90 tumors in 41/69 rats compared to 176 in 62/89 rats in the DMBA only group; this difference was significant ($P = 0.05$). The proportions of (1) growing, (2) static and (3) spontaneously regressing tumors in the M + DMBA groups was, resp., 24, 50 and 16; in the DMBA only groups results were 49, 70 and 49. (See also CRA 1(5):#848, 1963.)

64-37 EXPERIMENTAL STUDIES ON SYNOVIAL TUMOR. (E.) Mitomo, Y. (Dept. Path., Tokyo Med. Dent. U.). Bull. Tokyo Med. Dent. U. 10(2): 227-258, 1963.

Intraarticular and extraarticular implantation of 20-methylcholanthrene crystals (3 mg) in the right knee of 108 male Wistar rats resulted after 413 days in 27 tumors: 7 malignant synoviomas, 8 spindle cell sarcomas, and 12 polymorphous cell sarcomas. All 7 malignant synoviomas were located in intraarticularly implanted rats and revealed a histological pattern comparable with human malignant synoviomas of undifferentiated type. They began to appear on the 250th day, slightly later than the tumors in the extraarticularly implanted group. Although synovial cells are closely related to fibroblasts, their neoplastic nature is clearly seen when subjected to microscopic examination.

64-38 STUDIES OF NICKEL CARCINOGENESIS. THE SUBCELLULAR PARTITION OF NICKEL IN LUNG AND LIVER FOLLOWING INHALATION OF NICKEL CARBONYL. (E.) Sunderman, F. W., Jr. (Dept. Med., Jefferson Med. Coll., Philadelphia, Penna.) and F. W. Sunderman. Am. J. Clin. Path. 40(6):563-575, 1963.

Measurements were made of the subcellular partitions of nickel in the lung and livers of Wistar rats after treatment with nickel carbonyl by inhalation after both acute (0.60 mg/l of air for 60 min.) or chronic (0.030 mg/l of air for 30 min. 3x/wk. for 1 yr.) exposure. Nickel was determined by a sensitive UV spectrophotometric method. In normal rats nickel was located principally in the microsomal and supernatant fractions of lung and liver. In both treated groups, increases in nickel occurred predominantly in the microsomal and supernatant fractions of lung and liver. After chronic exposure, increased nickel was also observed in nuclear and mitochondrial fractions of the lung. (See also CRA 1(5):#830, 1963.)

64-39 CELLULAR MULTICENTRICITY OF THE ORIGIN OF CANCER. STUDIES WITH THE ASCITES HEPATOMA OF THE RAT. (Ger.) Yoshida, T. (Inst. Path., U. Tokyo). Deutsch. Med. Wschr. 88(46): 2229-2238, 1963.

Starting with 400 azo dye-induced rat hepatomas, 57 ascites hepatomas were obtained by transplantation. The earlier strains, going back to 1951, have already passed through over 500 generations.

Each of the ascites hepatoma strains is characterized by an easily recognizable "ascites figure", according to the distribution, size and shape of the cellular formations, which remains constant. The number of chromosomes of the hepatoma cells was studied in 15 of the 57 strains. The variation of the number of chromosomes per 100 cells ("modus") was found to be different in all 15 strains studied. No correlation could be found between the number of chromosomes and the rate of growth, transplantability or microscopic appearance of the tumors. The hypothesis according to which the origin of a tumor is to be found in a single cell is discussed. Whereas the transplantability and malignancy of the tumors usually increases with the number of passages, at least initially, examples are shown in which the reverse is true (AH 62) or in which no such changes take place (AH 7974). Both parameters can also vary independently from each other. Profound differences were found in the sensitivity of the various ascites hepatomas toward N-mustard, both *in vitro* and *in vivo*.

- 64-40 KINETIC STUDY OF THE INHIBITION OF GROWTH OF ROUS SARCOMA VIRUS AND CELLS BY 5-FLUOROURACIL *IN VITRO*. (E.) Golde, A. (Radium Inst., Paris) and P. Vigier. *Virology* 20(3):420-432, 1963.

Addition of 5-fluorouracil (FU) to cultures of chick embryo fibroblasts immediately after infection with Rous sarcoma virus (RSV; Bryan "high titer" strain) inhibited both cell growth and production of virus. Compared to noninfected controls, less FU was required to suppress growth and the conc. necessary to significantly inhibit virus production were higher than those sufficient to completely suppress growth of infected cells. In a kinetic study during the early period of growth, virus inhibition was seen only when FU was added before a certain time; no inhibition occurred up to 6 days after infection when FU was added later than 3 days after infection. The inhibition of growth of infected cells was not reversed by uracil and/or thymidine, added at the same time as FU, but cell growth was resumed following a period of contact of less than 24 hr. with FU. Addition of uracil (but not of thymidine) together with FU reversed the inhibition of virus production. These results suggest that FU inhibits the synthesis of RSV by replacing uracil either in viral RNA, or in nonviral RNA required for subsequent virus synthesis, but that it does not alter the viral genetic information or its association with the cell.

- 64-41 DEVELOPMENT OF SUBMICROSCOPIC CELLULAR INCLUSIONS IN MOUSE PULMONARY TUMORS. (Ger.) Klärner, P. (Inst. Path., U. Münster, Germany) and R. Giesekeing. *Frankfurt. Zschr. Path.* 73(2):138-148, 1963.

In 6-8-week-old A-strain mice, 2 i.p. inj. of

urethan (5% in saline, 1 mg/g) admin. over the course of 3 days, induced 1-4 electronmicroscopically demonstrable, pulmonary tumors per animal within 2 mo. Even at this early period, tumor cells showed numerous cytoplasmic inclusions lying close to the nucleus; at 6, 8, and 12 mo., intranuclear and/or extranuclear inclusions of virus-like structures were demonstrable in all animals examined. Observation also confirmed the presence of a progressive, developmental process in this respect. Similar phenomena were demonstrated at 7-11 mo. in spontaneously developing tumors in a control group.

- 64-42 ACID MUCOPOLYSACCHARIDES OF THE DERMIS GROUND SUBSTANCE DURING SKIN TREATMENT WITH 9,10-DIMETHYL-1,2-BENZANTHRACENE AND WITH CROTON OIL. (E.) Prodi, G. (Inst. Gen. Path., U. Bologna, Italy). *Brit. J. Cancer* 17(3):504-511, 1963.

For earlier work see CRA 1(1):#80, 1963. The skin of normal rabbits and rabbits treated topically twice a wk. for one mo. by 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.3% in acetone) or with croton oil (C; 2.5% in olive oil) was not appreciably changed in hexosamine (H) content, if related to tissue wt. (H as % of dry defatted skin = 0.33, 0.37, 0.36 for normal, DMBA and C skin), but was considerably increased when related to skin surface (H, mg/cm² = 0.10, 0.20, and 0.26, resp.). Skin wt./unit area was increased 2.07-2.65 x that of normal skin; the increase was greater for DMBA-treated tissue. The greater degree of hydration is attributed to increase of hyaluronic acid (HA), which contains glucosamine (GS), and chondroitin-sulfuric acid (CSA). The ratio of GS/galactosamine in crude mucopolysaccharides (MPS) hydrolysate for normal, DMBA and C skin was 1.01, 3.96, and 2.33, resp. The relative ratio of H (as HA) to CSA (obtained by analysis of Hyflo blocks from electrophoresis, HA less mobile than CSA) for MPS from normal, DMBA- and C-treated skin was, resp.: 1.22, 3.75 and 2.80. The ratio of the total amount of H extracted by 0.4 N NaCl and 1.2 N NaCl from MPS-cetylpyridium complexes were, resp.: 1.3, 2.7 and 2.3. Qualitative difference in mucopolysaccharides between treated animals and controls was not revealed. (See also CRA 1(1):#1890, 1964.)

- 64-43 THE INFLUENCE OF PSEUDOPREGNANCY ON BREAST TUMOUR INDUCTION BY METHYLCHOLANTHRENE IN IF OR F₁ HYBRID (C57Bl x IF) MICE. (E.) Marchant, J. (U. Birmingham Sch. Med., England). *Brit. J. Cancer* 17(3):495-503, 1963.

Female IF and F₁ hybrid (C57Bl x IF) mice were divided into 4 groups: olfactory lobes removed and then kept isolated; isolated; grouped virgins; or mated with vasectomized males. They were given cutaneous applications of 20-methylcholanthrene (MC; 0.5 ml of a 0.5% soln. in olive oil x 8 at fortnightly intervals) which resulted in

high incidence of breast tumors in survivors or all groups (IF--73% of 22, 93% of 15, 63% of 9, 95% of 20, resp.; F1--64% of 33, 75% of 28, 7% of 34 and 94% of 32, resp.). The rates of breast tumor induction (per 4 wk.) were similar for mice of the same genetic type, being between 0-60% for IF's and 25-45% for hybrids. In mice maintained with vasectomized males, the onset of breast tumors was several wk. earlier than in virgins maintained in groups of 5 or 6, although vaginal smears indicated similar high progesterone (P) levels in these 2 groups. When mice were maintained solitary (with or without prophylactic lobectomies) they remained very sensitive to tumor induction by MC, in spite of apparently reduced P levels. The conclusion drawn is that it is not always possible to correlate high susceptibility to breast tumor induction by MC in females of these strains with high levels of P. In the same groups, incidence of skin cancer was, resp.: IF--9% of 22, 47% of 15, 5% of 19 and 0% of 20; F1 hybrids--48% of 33, 5% of 28, 30% of 34 and 19% of 32. Incidence of leukemias (as described by Dunn, 1954) was, resp.: IF--41% of 22, 33% of 15, 16% of 19, 15% of 20; F1 hybrids--15% of 33, 43% of 28, 21% of 34, 9% of 32. Incidence of ovarian tumors was, resp.: IF--5% of 22, 7% of 15, 10% of 19, 0% of 20; F1 hybrids--12% of 33, 13% of 28, 21% of 34, 0% of 30.

4-44 TUMOR INDUCTION IN HYPOPHYSEAL GRAFTS IN RADIOHYDROECTOMIZED MICE; HYPOTHALAMICO-HYPOPHYSEAL RELATIONSHIPS. (E.) Hifton, K. H. (Dept. Radiol., U. Wisconsin Sch. Med., Madison). *Proc. Soc. Exp. Biol. Med.* 4(3):559-565, 1964.

Pituitary glands from intact or radiothyroidectomized (60-65 μ C of 131 I.p.) 6-8-week-old male LAF₁ mice were grafted (14-33 days after 131 I treatment) beneath the kidney capsules of similar intact and radiothyroidectomized recipients. In intact female hosts 14/17 pituitary grafts were larger than the host pituitary glands *in situ*; of these 10 weighed 8 mg or more as did 1 graft in thyroidectomized females. These grafts were shown by transplantation assay to be gonadotropin (MtT), not thyrotropic in nature. However, tumors weighing 8 mg or more were seen in 16/19 of the host pituitary glands *in situ*, and were typically thyrotropic (TtT) in behavior. Tumors were found in subcapsular grafts in intact or gonadectomized C57Bl/6 male mice and an unidentified small mass (5.5 mg) was found at the graft site in 1/18 thyroidectomized males. In thyroidectomized males, however, showed tumors of the pituitary glands *in situ*. It is tentatively concluded that the thyroid hormone deficiency resulting from radiothyroidectomy is not in itself sufficient to induce TtT tumors in pituitary grafts remote from the hypothalamus in C57Bl/6 mice.

64-45 CARCINOGENESIS. CARCINOGENICITY TESTS. (E.) Haddow, A., C. E. Dukes, F. J. C. Roe, B. C. V. Mitchley and J. L. Everett. Pp. 30-34 in *British Empire Cancer Campaign*. 40th Annual Report, 1962. Part II: Scientific Report. British Empire Cancer Campaign, London, S.W.1.

When 50 carcinogenicity tests were performed on groups of 20 mice each by s.c. inj. of the test compounds (dissolved or suspended in water or arachis oil), tumors at the inj. site and neoplasms elsewhere were produced by the following compounds: neo-ferrum saccharated iron-oxide (100 mg of elemental iron in 5 ml; 5-6 ml total), 4 sarcomas and 1 fibroma at site and 2 lymphomas; osmoferin (150 mg of iron as ferric-sodium gluconate complex in 2 ml; 1 ml total), 5 sarcomas at site and 1 lymphoma; ferrous glutamate (65 mg total), 3 sarcomas and none; iron hydrogenated dextran (50 mg Fe/ml; 57.5 mg total), 5 sarcomas at site and 1 lymphoma; ruthenium salt of tetramethylphenanthrene (25 mg total), well circumscribed squamous cell tumor of the skin (probably benign) at site and 3 lymphomas; 4-fluoro-1,2,5,6-dibenzanthracene (5 mg total), 5 sarcomas and none; magnesium phthalocyanine (25 mg total), adenoma of hair follicle origin at site with 2 hepatomas and 3 lymphomas, resp. All the remaining 37 compounds did not cause tumors at the inj. site, but all did produce lymphomas, and/or hepatomas as well as Leydig cell tumors (by 3 of the ferrocenes), pulmonary tumors, a skin carcinoma, squamous cell carcinoma of the bladder and abdominal cavity (1, by tetrabenzoporphyrin), spindle cell sarcoma of the hind leg (1, by micro-wax B.P. 160/258), and ovarian tumors elsewhere on the animals. Di(phenylisopropyl)ferrocene also produced an area of benign basal cell neoplasia on the facial skin as well as 7 lymphomas.

64-46 THE CARCINOGENICITY OF CADMIUM SULPHATE. (E.) Haddow, A., C. E. Dukes, F. J. C. Roe, B. C. V. Mitchley, R. C. B. Pugh and K. M. Cameron. Pp. 34-35 in *British Empire Cancer Campaign*. 40th Annual Report, 1962. Part II: Scientific Report. British Empire Cancer Campaign, London S.W.1.

Male rats inj. with cadmium sulfate (Cd; 0.5 mg/wk. x 10) developed sarcomas at the inj. site (13/20), and/or testicular atrophy and Leydig cell tumors (5/20). No local tumors developed in 20 mice given Cd (0.05 mg/wk. x 11) but some degree of testicular atrophy was seen in all the animals, and Leydig cell hyperplasia occurred in 5/20. In rats, single doses of 5 or 10 mg/kg of hydrated Cd (2.2 or 4.4 mg cadmium/kg) caused complete testicular atrophy within a few days. With 20 mg/kg of Cd, the animals were sick, but recovered, and with 2.5 mg/kg, the testicular atrophy was incomplete. Systemic examination of various organs indicated that atrophy of the testes affected both the seminiferous tubules and the interstitial cells, with subsequent regeneration

of the interstitial cells from the subcapsular epithelium, but not of the seminiferous elements. Castration cells in the pituitary were the only other detectable change. The effects obtained with the cadmium salt are thought to account for the results reported after s.c. inj. of rat ferritin (obtained by the cadmium salt precipitation method).

- 64-47 ON THE LATE INJURIES FOLLOWING OCCUPATIONAL INHALATION OF MUSTARD GAS, WITH SPECIAL REFERENCES TO CARCINOMA OF THE RESPIRATORY TRACT. (E.) Yamada, A. (Dept. Path., Hiroshima U. Sch. Med., Japan). Acta Path. Jap. 13(3):131-155, 1963.

In an apparent continuation of CRA 1(4):#641, 1963, the author reports the patho-anatomical studies on the former workers of a poison gas factory which mainly produced mustard gas (bis(2-chloroethyl)sulfide) and Lewisite (dichloro(2-chlorovinyl)arsine) during 1937-1944. Of 172 cases surveyed over the yr. 1933-1962, the cause of death was cancer of the respiratory system in 28 (17 bronchus, 6 larynx, 3 pharynx, 1 trachea, 1 nasal sinus, 1 tongue), of the digestive system in 18 (9 stomach, 4 liver, 3 esophagus, 2 intestine) and skin in 2; the majority of the lesions originated in the upper respiratory tract. The mortality rate of respiratory cancer among these workers was much higher (16.3%) than that of non-exposed inhabitants of the same area (0.3-0.5%). Histology of 23 cases of respiratory cancer showed 16 squamous cell carcinomas and 7 undifferentiated cell carcinomas; no adenocarcinomas were found. Among 291 workers who were directly exposed to the gas, examination showed that 90.7% are still suffering from severe chronic bronchitis and 54.8% from skin changes as compared to 17.2% and 0%, resp., for non-exposed inhabitants of the same area; of 75 business clerks in the same factory, the corresponding figures were 46.7% and 14.7%, resp. The period of exposure to mustard gas in this series of respiratory cancer was 7-9 yr. and the latent period for carcinoma induction was 17-20 yr. The author notes that no morphological transition from metaplasia to carcinoma and no hypertrophy of the adrenal were seen.

- 64-48 NEOPLASMS OF THE RESPIRATORY TRACT AMONG POISON GAS WORKERS. (E. and Jap.) Wada, S. (Dept. Int. Med., Hiroshima U. Sch. Med., Japan), A. Yamada, Y. Nishimoto, S. Tokuoka, M. Miyanishi, S. Katsuta and H. Umisa. Hiroshima Igaku (J. Hiroshima Med. Assn.) 16(8):728-745, 1963.

A similar but not identical report of the preceding abstract (CRA 2(1):#47, 1964). The authors have found that the major manifestations of the skin and respiratory system in those employees who had worked with mustard gas (155), Lewisite (12) and other gases (53) as well as those

engaged in desk work (75) were: abnormal skin pigmentation or scars in 61.9%, 75%, 20.8% and 14.7%; productive cough in 88.4%, 66.7%, 47.2% and 68.0%; and bloody sputum in 40.6%, 25%, 13.2% and 13.3%, resp.

- 64-49 OBSERVATIONS ON THE EFFECTS OF TOBACCO SMOKE ON THE ORAL MUCOSA. (E.) Borota, A. (Dept. Derm., N.Y. Med. Coll., New York), J. L. Morse and M. Owrandi. J. Am. Geriatr. Soc. 12(1):67-70, 1964.

In a 4-part study, examination of the oral cavity of 1,529 geriatric patients, 9 cases of oral mucosal cancer were found among 1,006 smokers while only 1 case was seen among the 523 non-smokers. These pts. represented a fairly homogeneous group with similar backgrounds and identical nutritional factors, and were available for follow-up. In part 4 of the study (examination of 750 pts.) 4 smokers with squamous cell cancer all smoked cigarettes and showed leukoplakia; 2 were in what are judged potentially dangerous occupations (carpenter and artist, painter).

- 64-50 URINARY 11-DEOXY-17-OXOSTEROIDS IN BRITISH AND JAPANESE WOMEN WITH REFERENCE TO THE INCIDENCE OF BREAST CANCER. (E.) Bulbrook, R. D. (Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, W.C.2), B. S. Thomas, and J. Utsunomiya. Nature (London) 201: 189-190, 1964.

A study of 59 British and 24 Japanese women (all living in Tokyo) was made to determine if the decreased incidence of breast cancer in Japanese women (12.5% that of British or N. American women) was related to endogenous androgen levels. Total 24 hr. urinary excretion of 11-deoxy-17-oxosteroids for Japanese and British women was resp., 1.79 mg and 3.41 mg. However, the Japanese women were considerably shorter and lighter than the British and if the steroid results were expressed in terms of creatine excretion the striking difference in excretion rates disappeared. Japanese women did excrete more androsterone (5 α) relative to etiocholanolone (5 β) than did the British women. The mean 5 α /5 β ratio in the former was 1.3 and in the latter 1.0 ($t = 3.25$; $P < 0.01$). Since this ratio is markedly affected by thyroid function these results may, according to the authors, indicate that thyroid function is greater in Japanese than in British women. Since thyroid disease has been reported to affect the incidence of breast cancer, the authors postulate that the difference in 5 α /5 β ratios between the populations may be relevant to the difference in incidence.

- 64-51 EARLY EFFECTS OF HYDROCARBONS ON MAMMALIAN SKIN. (E.) Bock, F. G. (Roswell Park Mem. Inst., Springville, N.Y.). Progr. Exp. Tumor Res. 4:126-128, 1964.

in a review (82 references) and discussion of the penetration of hydrocarbons into the skin (see CRA 1(3):#396, 1963), the intermolecular reactions of hydrocarbons and the effects of hydrocarbons on organized skin structures, the author presents additional data on the role of the solvent and skin structure in penetration. There was no significant decrease in the penetration of 3,4-benzpyrene (BP) into the skin when the conc. was reduced (from 1.0%-0.1%), but penetration was increased by the addition of 1% or 2% mineral oil. Pretreatment of adult C3H/St mice with 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.03% in benzene, 2x/day x 3) to destroy the sebaceous glands, resulted in higher penetration of 1% BP in benzene containing 1% mineral oil (40.1 µg/g) as compared to benzene (0.25 ml twice daily) pretreatment (25.5 µg/g). Based on the data of S. Crouch and B. Nestler, molecular structure also affects penetration: hydrocarbons with few rings and no side chains penetrate best; methyl substitution for a hydrogen thickens the molecule and slows down penetration; alkyl substitution favors solubility and increases penetration. Studies of a possible intermolecular reaction between hydrocarbons and sulfhydryl compounds were conducted by adding heptanethiol (RSH) and glutathione (GSH) to the hydrocarbons. *In vitro* it was shown that polycyclic carcinogens generally do not react directly with the -SH group. With regard to subcellular particles, there is some evidence that alterations of mitochondrial function may be directly related to tumor formation, while stimulation of rat-liver microsomes in enzyme synthesis is well documented. *In vivo* hydrocarbons (in conc. with sebaceous-gland suppression activities of 3, 1 and 1/3 U/ml) were applied in 0.25 ml of acetone to 18 experimental groups of 30 ICR Swiss mice 4 times/wk. Results indicated a close parallel between carcinogenic activity and sebaceous-gland suppression index (10,000 for methylcholanthrene, DMBA, and methyl-BP; 3,000 for BP and dibenzanthracene; 1,000 for benzanthrane (BA)). With doses producing identical sebaceous-gland effects, DMBA produced more tumors, while BA produced consistently fewer tumors than the other compounds.

52 HISTOCHEMISTRY OF EXPERIMENTALLY INDUCED LEUKOPLAKIA AND CARCINOMA OF THE HAMSTER BUCCAL POUCH. (E.) Santis, H. (Dept. Oral Path., Tufts U. Sch. Dent. Med., Boston, Mass.), G. Shklar and H. H. Chauncey. *J. Nat. Cancer Inst.* 17(2):207-218, 1964.

Repeated application of a 0.5% soln. of 9,10-dimethyl-1,2-benzanthracene in acetone to the buccal pouch of 45 Syrian hamsters (60-days-old) resulted in a large number of epidermoid carcinomas whose altered "enzyme patterns" were compared with those of normal mucosal epithelium. The following responses were observed after periods of 10 wk. (Group A), 16 wk. (Group B), and 24 wk. (Group C), resp.: animals with normal pouches 1, 0, 0; with chronic inflammation

2, 0, 0; with chronic inflammation and epithelial hyperplasia 4, 2, 3; with hyperkeratosis and dyskeratosis 5, 6, 3; with well differentiated epidermoid carcinoma 2, 6, 7; with anaplastic epidermoid carcinoma 0, 0, 2; with papilloma 1, 1, 0. Increased acid phosphatase, alkaline phosphatase and beta-D-galactosidase activity and decreased esterase activity characterized the epidermoid carcinomas. A transitional zone, characterized by hyperkeratosis and dyskeratosis and similar to human oral leukoplakia, was noted in proximity to the carcinomas in 2 animals of Group A, 4 of Group B and 5 of Group C. These zones presented enzyme "activity patterns" similar to, but less reactive than, those exhibited by the carcinoma.

64-53 SUBCUTANEOUS NEOPLASMS INDUCED BY TRYPAN BLUE. (E.) Brown, D. V. (Dept. Path., U. Washington Sch. Med., Seattle). *Lab. Invest.* 12(12):1221-1227, 1963.

A more detailed account of CRA 1(7):#1284, 1963. The dye-induced s.c. tumor was also successfully transplanted.

64-54 STUDIES ON SERUM PROTEIN CHANGES AND ORGAN DYE CONCENTRATIONS IN TRYPAN BLUE CARCINOGENESIS. (E.) Brown, D. V. (VA Hosp., Seattle, Wash.), L. M. Norlind, A. Adamovics and A. Bowen. *Proc. Soc. Exp. Biol. Med.* 114(2):290-293, 1963.

In Wistar rats, single s.c. inj. of trypan blue (TB; 20 mg/100 g) produced a prompt reduction in total serum proteins during a 9-day period due largely to a decrease in the albumin fraction. During this same period, all the globulin fractions increased with the most marked change in the γ -globulin. Histiocytic liver tumors appeared from 28-100 days after 15 biweekly inj. of TB (10 mg/100 g), but the total serum proteins, measured 1-3 mo. after the last inj., were reduced with no notable change in the proportion of the protein fractions. The hypoproteinemia in animals with reticuloendothelial tumors was attributed to the advanced stage of neoplasia. An "abnormal" band between α^1 and α^2 previously seen in the serum of rats only after TB treatment was also seen in the serum of untreated animals; the dye treatment increased the incidence from 15% in untreated animals to 50% in experimental animals. The incidence and conc. of the band was not increased in tumor bearing animals. It was postulated that tumors of the liver from TB might be due to release of free dye or formation of metabolic breakdown products.

64-55 DISCUSSION ON EXPERIMENTAL TUMORS; CRITERIA FOR DESIRABLE TUMOR SYSTEMS. (E.) Schirmer, H. (Johns Hopkins U. Sch. Med., Baltimore, Md.). *Nat. Cancer Inst. Monogr.* (12):405-406, 1963.

After establishment of a possibly inactive and atrophic but normal glandular epithelium in a dog prostate by ligation of the blood supply to 1 lobe, a saline suspension of 20-methylchol-anthrene (MC) was inj. into each lobe. Some glands showed squamous metaplasia, but principal results were acute and chronic inflammation with abscess formation in some instances. No cancer has been found in a 1.5 yr. follow-up. Intact and orchiectomized mature Wistar rats on normal and high carbohydrate diets receiving α -estradiol (25 mg 3x/wk. s.c.) were admin. a silk suture soaked in MC (dissolved in sesame oil) through the ventral prostate. Carcinomas (squamous cell) developed in the prostates of 38/72 after latent periods of 6-12 mo. These tumors caused urinary tract obstruction; they metastasized and were transplantable, but they were not endocrine-sensitive. The dietary and endocrine influences seem to be statistically insignificant.

64-56 DIFFERENCE BETWEEN THE PARENTAL STRAIN AND THE F_1 HYBRID IN THE ISOIMMUNE REACTION TO TUMOURS. (E.) Koldovský, P. (Inst. Exptl. Biol. Genet., Czech. Acad. Sci., Prague) and J. Bubeník. Folia Biol. (Praha) 9(6): 420-423, 1963.

Male and female CBA mice and F_1 (A x CBA) hybrids with benzpyrene (BP; 1 mg s.c.)-induced tumor designated Bp 7/CBA were preimmunized with Bp 7/CBA (0.3 ml of 30% cell suspension lethally irradiated with 20,000 r) and immunized 2x at a 3-wk. interval with living tumor cells (sub-threshold dose of 3.10^3 cells). In vitro incubation of sera taken 10 days after the last immunization showed that the CBA mice did not produce cytotoxins in detectable amounts (cytotoxic index of 0.24; normal sera control = 0.29), while the F_1 hybrids showed a cytotoxic index of 0.48; a similar cytotoxic index (0.50) was seen with sera taken from CBA mice after rejection of Bp 7/CBA tumor. When the CBA and F_1 hybrid controls and preimmunized (2 x 30 mg irradiated Bp 7/CBA cells) animals were challenged with living tumor cells (1×10^4), only 1/30 preimmunized hybrids died with a progressively growing tumor (control, 12/12), whereas 13/32 CBA mice died (controls, 13/13). When the reactivity of both types of preimmunized mice was compared by challenge with living tumor cells, 10^4 cells killed no F_1 hybrids and 4/10 CBA mice; 10^6 cells, however, killed only 2/10 F_1 hybrids and almost all (9/10) of the CBA mice. The results obtained indicate clearly that F_1 hybrids show greater resistance to benzpyrene-induced tumors than parental strains. (For related studies, see CRA 1(4):#762, #763, #764, 1963.)

64-57 STUDIES ON THE EFFECT OF IRRITANT VAPORS ON CILIARY MUCUS TRANSPORT. I. PHENOL AND CIGARETTE SMOKE. (E.) Bernfeld, P. (Bio-Res. Consult., Inc., Cambridge, Mass.),

C. W. Nixon and F. Homburger. Toxic. Appl. Pharmacol. 6(1):103-111, 1964.

A method was developed to study the effects of tobacco smoke and phenol upon frog cilia; measurement was made of mucous flow rates in the frog (*Rana pipiens*) esophageal tissue preparations, in the presence of 0.00625% sodium adenosine triphosphate in frog Ringer's soln. It was concluded that smoke from a filter cigarette had considerably less cilia-inhibitory effect than smoke from an unfiltered cigarette. The effect was considered statistically significant and was attributed, at least in part, to selective removal of phenols from the smoke by the cigarette filter. Pure phenol vapor had little or no effect on ciliary activity but in the presence of smoke from a filter cigarette it became markedly cilia-inhibiting (probably in conjunction with the particulate phase of cigarette smoke). Phenol vapors did not potentiate the effect of smoke from a non-filter cigarette, and it was concluded that smoke from a non-filter cigarette is already saturated with phenol.

64-58 CONTRIBUTION TO THE PROBLEM OF THE CARCINOGENIC POWER OF TOBACCO. (Fr.) Alexandrov, K. and P. Raitchev. C. R. Acad. Bulgare Sci. 16(3):329-332, 1963.

A total of 180 rats aged 2-5 months were subjected for a period of 1 yr. alternately to the action of cigarette smoke for 5-6 seconds, followed by clean air for 8-10 seconds. A total of 73 rats died within the first 2 mo. from the toxic effects of smoke inhalation. The experiment was then modified to include 2 cigarettes daily, increasing periodically the number of cigarettes to 3 daily, and back to 2. Among the 68 survivors, after 1 mo. of treatment, non-specific chronic inflammatory modifications of the peribronchial structures were evident which became more prominent after 3-4 mo. After 5 mo., papillomatous modifications of the mucosal epithelium were observed, accompanied by mucus formation and planocellular metaplasia. One animal, after 6 mo. of smoke inhalation, exhibited a tumor of glandular structure. In the animals subjected to smoke inhalation for 7 mo., there was enhanced growth of the epithelium which, in addition to a papillomatous character, acquired a glandular structure with lesions of the basal membrane. One animal, after 8 mo., showed infiltration of the epithelium with mucosal formations, resulting in a glandular carcinoma.

64-59 CONSIDERATIONS ON THE PROBLEM OF CARCINOGENESIS AT THE SITE OF CHRONIC INFLAMMATION. (Ger.) Ehlers, G. (Clin. Dermatol., U. Giessen, Germany). Berufsdermatosen 11(6): 332-341, 1963.

A case is reported of a pt., aged 50, who developed a basal cell epithelioma on the left side of the

in, an area which 14 yr. earlier (while a prisoner of war) was the site of an alleged mycotic infection. During the intervening yr. treatment of this area of chronic inflammation involved the use of Arning's tincture and X-irradiation, both of which were considered as contributing carcinogenic factors. A claim for compensation to the patient was recognized.

60 THE EFFECT OF CORTISONE ON CARCINOGENESIS AND METASTATIC SPREAD OF AUCTIONARY TUMORS. (E.) Ghose, T. (Dept. Path., Med. Bldg., Forester Hill, Aberdeen, Scotland). *Indian J. Med. Sci.* 17(12):921-925, 1963.

The 2-5 month-old inbred Swiss mice were treated with cortisone (C; 0.5 mg/day x 6 i.p.), followed by 20-methylcholanthrene (1 mg in olive oil s.c.) and C (40 inj. of 0.5 mg over 46 days). In the treated animals, 7/24 developed spindle cell sarcomas at the inj. site (mean latent period 124.7 days), 5/24 had lung tumors only and 5/24 had metastases in 5 different organs. The incidence in controls was, resp.: 12/24 (1/12 also had a lung tumor) with a mean latent period of 144 days, 0/24 and 5/24 (1/5 of the tail, 4/5 in different organs). The C-treated mice had a lower tumor growth index (based on the final wt. of the tumor in g x 100/duration of tumor in days) than the controls. The age at death of the treated mice was 6.0-14.0 mo. as compared to 1-13 mo. for the controls.

61 THE RESPIRATION OF MOUSE EPIDERMIS AFTER A SINGLE APPLICATION OF 3-METHYLCOLANTHRENE IN BENZENE. (E.) Iversen, O. H. (Inst. Gen. Exptl. Path., U. Oslo, Norway) and D. Laerum. *Acta Path. Microbiol. Scand.* (1):90-92, 1964.

The oxygen consumption/mg of dry hairless mouse epidermis at different time intervals after a single application of a 1% soln. of 20-methylcholanthrene (MC) in benzene was: 2 hr. = 1.19 ratio (values of treated/untreated areas of epidermis from the same animal); 4 hr. = 1.095 ratio; 8 hr. = 1.013 ratio; 16 hr. = 0.891 ratio; 24 hr. = 0.799 ratio. As shown previously, the melanin deposition in epidermis increases during the first 24 hr. after a MC application, while the O_2 consumption showed a decreasing curve. See also CRA 1(2):#243, 1963 and *ibid.*, 2(1):100, 1964.)

62 THE METABOLISM OF TRYPTOPHAN IN PATIENTS WITH BLADDER CANCER AND OTHER UROLOGICAL DISEASES. (E.) Benassi, C. A. (Inst. Pharm. Chem., U. Padua, Italy), G. Perissinotto and G. Allegri. *Clin. Chim. Acta* 8(6):822-831, 1963.

A study on the spontaneous urinary excretion

of tryptophan metabolites (kynurenine, 3-hydroxykynurenine and 3-hydroxyanthranilic acid) in 201 pts. with cancer of the bladder, 55 pts. with cancer of the genitourinary tract (extra-bladder) and 112 with non-neoplastic urinary diseases, abnormal excretion of the above metabolites occurred not only in 60 of the bladder cancer pts. but also in 28/55 genito-urinary, extra-bladder, cancer pts., and in 17/112 pts. with non-neoplastic urological diseases as well as in 19/32 kidney tumor pts. Spontaneous excretion of kynurenine was slightly decreased in some pts., but the abnormal excretion was never completely inhibited, by admin. of pyridoxine (120-300 mg/day p.o.) to 9 bladder cancer pts. for periods of 6-22 days. When L-tryptophan (100 mg/kg body wt.) was admin. to 4 bladder tumor pts., these pts. appeared to excrete 1.5x more tryptophan derivatives than normal controls.

64-63 BIOCHEMICAL STUDIES ON THE METABOLISM OF THE TUMOR BEARING ANIMALS. II. RESEARCHES FOR THE AMINO ACIDS IN THE URINE OF THE RATS FED ON THE DAB-RICE. (Jap.) Takatori, K. (Gifu Coll. Pharm., Japan), I. Ishiguro, S. Asano, H. Kuzuya, M. Okamoto, R. Kono and K. Morishima. *Yakugaku Zasshi (J. Pharmaceutical Soc. Jap.)* 83(10):981-987, 1963.

Rats were fed on a rice diet containing 0.06% of dimethylaminoazobenzene (DAB) and their urine was examined by two-dimensional paper chromatography. After DAB there was an increase in the number and amounts of free amino acids excreted. When determined over a period of 16 wk. after start of DAB, there was markedly increased excretion of tyrosine and kynurenine which coincided with the period of active tumor formation. During this period there was no great variation in the amount of total N in the urine.

64-64 CARCINOGENIC RESPONSE OF THE SYRIAN GOLDEN HAMSTER TREATED AT BIRTH WITH 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Lee, K. Y. (Inst. Med. Res., Chicago Sch. Med., Ill.), B. Toth and P. Shubik. *Proc. Soc. Exp. Biol. Med.* 114(3):579-582, 1964.

Newborn Syrian golden hamsters were given 9,10-dimethyl-1,2-benzanthracene (DMBA; 100, 200 or 1000 μ g in tri-n-caprylin, single s.c. inj. to the interscapular region). Of those treated with 200 μ g and 1000 μ g DMBA, only 3/50 and 4/53, resp., survived; all these animals developed multiple melanotic skin tumors. The 3 females of the 1000 μ g group developed skin papillomas (1 each), s.c. sarcomas (2 had 2 each) and 1/3 had a malignant lymphoma. Of the males and females treated with 100 μ g of DMBA, the type of developing tumor and the av. latent period were: dermal melanocytomas in 88.2-91.3% after 14-17 wk. (melanotic spots also occurred); s.c. (mainly on the back) spindle cell sarcomas in 78.2-80.2%

after 15-22 wk. (metastases to the lungs and lymph nodes occurred in 13 animals); malignant lymphomas in 1 male and 1 female after 36 and 42 wk., resp.; and other tumors such as adenocarcinoma of the breast (1), papilloma of the esophagus (1), angiosarcoma of the kidney (1), and hemangioma of the lymph node (1). The controls developed a few s.c. sarcomas, malignant lymphomas and some other tumors.

64-65 BIOLOGICAL ACTION OF BERYLLIUM. RE-ACTION OF THE MONKEY TO INHALED AEROSOLS. (E.) Schepers, G. W. H. (Inst. Forensic Med. Toxic., Newark, Del.). Industr. Med. Surg. 33(1):1-16, 1964.

When groups of 4 female Macacus mullata monkeys were exposed during 6 daylight hr. to aerosols of equimolecular quantities of 3 beryllium compounds (5.2-5.6 μg of Be/foot^3), BeF_2 was most toxic and BeHPO_4 least toxic; BeSO_4 was intermediate. After exposure to BeHPO_4 of 66 μg , 363 μg and 2.75 mg/foot^3 (Be ratios of 1:5.7:41.9) the two higher conc. killed all monkeys within 92 and 20 days, resp. The BeF_2 and the 2 higher conc. of BeHPO_4 caused severe and universal pulmonary reactions and changes in many organs; some of these changes were reversible but others were progressive. The only neoplasm was a small pulmonary tumor which developed in 1 monkey 82 days after exposure to a high conc. of BeHPO_4 .

64-66 FURTHER STUDIES ON CARCINOGENIC ACTION OF 4-HYDROXYAMINOQUINOLINE 1-OXIDE. (E.) Shirasu, Y. (Inst. Physical Chem. Res., Tokyo, Japan). Gann (Jap. J. Cancer Res.) 54(4):487-495, 1963.

Female mice of inbred ddOM strain (Group A) received 15 s.c. inj. (1/wk. with interval of 3 wk. between inj. 5 and 6) of 0.1 ml of 0.05% (= 0.5 mg/mouse) suspension of 4-hydroxyaminoquinoline N-oxide (4-HAQO) in physiological salt soln. with added Tween 80. Group B received 10 s.c. inj. (1/wk.) of 0.1% suspension of the same carcinogen (0.1 mg/mouse). During the observation period of 8-9 mo., 8/11 mice of Group A showed tumors of the following types: 4 fibrosarcoma, 1 carcinosarcoma, 1 carcinoma of the sweat gland, and 3 papilloma (1 mouse dead of leukemia had both a fibrosarcoma and a papilloma). In Group B, 10/15 mice showed 4 fibrosarcoma (1/4 associated with a papilloma), 2

rhabdomyosarcoma, 2 squamous cell carcinoma, 1 carcinoma of the sweat gland, and 2 papilloma. After only 3 inj. (1/wk.) of 1.0 ml of 0.1% (= 1 mg/rat) suspension of 4-HAQO + Tween 80, young, female, non-inbred, Wistar rats developed 5/10 fibrosarcomas in a 4-8-mo. period. Tumor tissue from 2 mice in Group A and B was successfully transplanted in ddOM mice. Lung adenomas were seen in 4 mice of Group A sacrificed on day 270, 1 animal in Group B sacrificed on day 240 and 1 control sacrificed on day 270; no rats showed lung tumors, while mammary cancer occurred in 1 mouse (adenocarcinoma) and 2 rats. Lymphatic leukemia occurred in 1 animal from each group. The following compounds did not induce tumor formation and did not cause tissue reactions after 6-10 mo.: 4-HAQO acetate, 3-nitroquinoline N-oxide, 4-azidoquinoline N-oxide, 4,4'-azoquinoline 1,1'-dioxide, 4-chloroquinoline N-oxide, 4-aminoquinoline N-oxide, 4-nitropyridine N-oxide, and 4-hydroxyaminopyridine N-oxide.

64-67 THE ABILITY OF CARCINOGENIC SUBSTANCES TO LEND ELECTRONS AS A FACTOR IN CHEMICAL CARCINOGENESIS. (Ger.) Damerau, W. (German Acad. Sci. Berlin) and G. Lassmann. Arch. Geschwulstforsch. 22(1/2):200-209, 1963.

Studies of charge-transfer-reactions in 9 azo-benzene compounds, β -naphthol orange, and Congo red showed no significant differences between the electron-lending capacities of carcinogenic and non-carcinogenic compounds. The authors suggest that the ability of the benzoquinones to reduce the carcinogenic activity of hydrocarbons may be explained on the ground that they are active electron-receptors, thus reducing the effect of the hydrocarbons on cells exposed to them.

64-68 NITROSAMINES. (E.) Boyland, E., J. W. Gorrod, B. C. V. Mitchley and F. J. C. Roe. P. 34 in British Empire Cancer Campaign. 40th Annual Report, 1962. Part II: Scientific Report. British Empire Cancer Campaign, London, S.W.1.

Nitrosoanabasine and nitrosonornicotine were synthesized and qualitative and quantitative methods for their detection have been developed. Nitrosoanabasine is being tested for carcinogenicity in rats and has failed to induce tumors to date. Nitrosopiperidine has produced some esophageal tumors in rats.

See also abstract nos.: 6,71,133

VIRAL CARCINOGENESIS

69 CYTOLOGICAL INVESTIGATIONS OF THE PROPAGATION OF SV-40 VIRUS IN TISSUE CULTURES. (E.) Signer, E. (Inst. Hygiene, Albert-Ludwigs-Freiburg i. Br., Germany), J. Müller and Maass. *Zschr. Hyg. Infektionskr.* 149(3): -254, 1963.

The propagation of SV40 virus in kidney tissue cultures of *C. aethiops*, *M. cynomolgus* and new-born rabbits was studied by virological, microscopic and electron microscopic methods. The cytological changes observed were characterized by hyperplasia of the nucleus, enlargement of the nucleolus, the formation of intranuclear Feulgen-positive inclusion bodies and the formation of cytoplasmic vacuoles. The nuclear hyperplasia in infected cells was found to be statistically significant. The electron microscope revealed the presence in the inclusion bodies of virus particles in large numbers. In the late stages of the infection, virus particles in paracrystalline formation were seen occasionally in the cytoplasm of markedly changed cells. The formation of intranuclear inclusion bodies and of cytoplasmic vacuoles was also observed in infected kidney tissue cultures of *M. cynomolgus*, but they occurred later and more rarely than in the case of *C. aethiops*. The virus did not grow in the rabbit kidney tissue cultures.

70 CELL DIVISION AND CANCER. (E.) Gongdon, C. C. (Oak Ridge Natl. Lab., Tenn.). *Nature* 142:252-260, 1963.

An international symposium held in Lima, Peru, Cali, Colombia, A. Pardee suggested that the point of action of carcinogens may be on the surface properties of the cell; and H. Kalckar extended this concept by suggesting that the polypeptides may subserve the "social functions" of the cell and pointing out that the lack of particular antigens on cell surfaces may be related to an epimerase defect (see CRA 1(12):#2222, 1963). E. de Robertis then stated that electron microscopy has established the basic unit of the chromosome as a filamentous, macromolecular component or microfibril, which may well be a single polypeptide molecule; while D. M. Prescott suggested that control of DNA synthesis (which may be the point at which carcinogens act) may reside in each gene itself. R. P. Perry suggested that carcinogens may upset the usual control of cell division by interfering with the normal function of the nucleolus, an RNA-containing organelle intimately associated with specific chromosomal proteins. D. Mazia discussed intracellular metabolic control mechanisms, emphasizing that a special mechanism designed for control of the enzyme has been demonstrated, which has nothing to do with the enzyme's concerned with enzymatic function. A. Pardee stated that repressor genes have now been shown to control the functioning of operator genes, being able to "turn a gene on or off" for an extended

period, thus sometimes simulating a mutation. S. E. Luria reported that viruses can produce permanent changes in cells by initiating new synthetic processes directed by the viral genes, or by establishing new regulatory controls on the function of cellular genes. He also reported that viruses are capable of mass repression of gene action by turning off entire blocks of host genes. He also described the existence of helper viruses, which complete the action of a defective virus such as that seen in Rous sarcoma. S. Rogers said that the Shope papilloma virus brings new antigens to the papilloma, plus new metabolic information in the form of a unique papilloma arginase (see also CRA 1(3):#459, 1963). L. F. Lamerton reported that stem cells from various cell renewal systems could be made to proliferate under continuous irradiation: those of the small intestine were most resistant to irradiation and those of the testis most sensitive. C. Pavan presented evidence that in some Diptera, where DNA synthesis occurs without cell division, irradiation may actually stimulate DNA synthesis. H. S. Kaplan and A. C. Upton both gave progress reports on induction of leukemias with filterable agents presumably released by radiation, suggesting a train of intracellular events in which a virus might be incorporated into the genome of the target stem cell. M. C. Brown reported follow-up studies of 13,000 persons with spondylitis who were irradiated in 32 British radiation centers: 95% of those developing chronic myeloid leukemia subsequently showed the Philadelphia chromosome. Both stable and unstable chromosomal abnormalities were seen in these pts., the former persisting for as long as 20 yr. Upton added that studies he and N. Wald were making of transmitted myeloid leukemia in mice had shown a typical, extra chromosome in all cases thus far examined, including cases transmitted by cell-free supernatant fluid. P. Mori-Chavez and A. Stella reported that cancer induction and metastasis were different at high altitudes than they were at sea level and that cancer occurs at high altitudes in Peru. A. Tannenbaum presented evidence suggesting that all carcinogens may be multi-potential as concerns the type of tumor induced.

64-71 INHIBITION BY URETHAN (ETHYL CARBAMATE) OF VIRUS INDUCTION OF LEUKAEMIA IN C3H MICE. (E.) Law, L. W. (NCI, Bethesda) and A. Precerutti. *Nature (London)* 200:692-693, 1963.

Mice of both sexes, 24-72 hr. after birth, were given urethan (U; s.c.), either in a single dose of 1 mg/g body wt., or the same dose given weekly for 4 consecutive wk.; observations were made at 10 mo. Low-leukemic strain C3Hf/Lw mice did not develop lymphocytic neoplasms at either dose level; most mice had multiple hepatomas. Spontaneous rate for leukemia in this strain is about 10% but rarely occurs before 12 mo.; hepatomas occur with moderate frequency among males, but usually beyond a year of age. In the high-leukemic strain

C3Hf*/Lw, in U-treated mice at both doses there was a striking inhibition of lymphocytic neoplasms, principally of thymic origin. In the few survivors there was a high frequency of hepatoma. Among all groups, lung adenomas were rare. A group of BALB/c mice given a single dose of U at 24-72 hr. failed to develop any leukemia when killed at 10 mo. No hepatomas were found but 89% had multiple lung adenomas. These results and some published studies indicate that the induction of leukemia (or other neoplasms) is not a general phenomenon but is apparently quite dependent on the genotype of the animal.

- 64-72 ELECTRON MICROSCOPIC STUDY OF VIRUS IN THE C58 MOUSE WITH SPONTANEOUS LYMPHOID LEUKEMIA. (Jap.) Ota, Z. (Dept. Int. Med., Okayama U., Japan) and N. Suzuki. Rinshō Byōri (Jap. J. Clin. Path.) 11(7):369-370, 1963.

Upon electron microscope examination, grouped as well as isolated virus particles were found in leukemic and reticulum cells of the lymph glands and spleens of C58 mice with spontaneous lymphoid leukemia. These intracellular particles were round to oval in shape, 70-90 mμ (av. 80 mμ) in diameter. The particle is outlined by 2 membranes. The nucleoid had a diameter of 50 mμ and appeared to contain 3-4 tubular structures. The virus appeared to undergo replication at cell membranes. These findings were close to those observed in SL and AkR strain mice.

- 64-73 TRANSMISSION OF X-RAY INDUCED LA VUFB LEUKEMIA BY CELL-FREE FILTRATE. (E.) Libánský, J. (Inst. Hemat. Blood Transf., Lab. Electron Microscopy, Prague, Czech.), M. Lázníčka, J. Libánská and J. Jirásek. Neoplasm (Bratisl.) 10(5):487-505, 1963.

LA VUFB leukemia, which originally was induced by X-rays, after over 170 passages by means of pooled liver and spleen homogenized cell suspensions in C57 Black mice, was transmitted by a cell-free filtrate prepared from leukemic spleen and node. This leukemia (CFF LA VUFB), transmitted in the same way, is now in the 3rd passage in both newborn and adult mice of the same strain; 50% of the 24 young mice in the 1st passage became leukemic (latency period 6-12 mo.). The type of leukemia induced is the same (lymphatic) and differs from the parent strain only by the degree of generalized enlargement of the nodes and thymus. CFF LA VUFB leukemic cells under the electron microscope revealed, in slightly edematous mitochondria, incomplete, irregular, partly deformed cristae with numerous little osmophilic granules attached to them. Degenerated mitochondrial forms with double membrane and disintegrated cristae and osmophilic inclusions were also observed. Experiments in which an attempt is being made to transmit CFF LA VUFB into another strain (CBA) have not proceeded long enough for evaluation; after 9 mo. 2/66 have developed leukemia which is only 1% more

than the spontaneous rate. An attempt to transmit CFF LA VUFB to C57 Black mice through cell transplantation (0.2 ml spleen and lymphatic suspension, i.p.) in 5 adult males and 5 young females produced no leukemias in 5 mo. In two similar experiments, after 4-8 mo., leukemia was demonstrated in 5/20 and after 9 mo. in 12/17 adult mice. Application of cell-free filtrate from CFF LA VUFB to adult C57 Black mice prior to transplantation of LA VUFB cells led to a somewhat faster course of leukemia (av. latency 1 day less) in contrast to a control group treated with cell-free filtrates from normal spleen.

- 64-74 SE POLYOMA-VIRUS TUMOR AND THE TEETH. (E.) Fleming, H. S. (Howard U. Coll. Dent., Washington, D. C.). J. Dent. Res. 42(6):1405-1415, 1963.

Two litters of Swiss hybrid mice, within 12 hr. after birth, were inoc. with 0.2 ml of supernatant of a mouse embryo tissue culture infected with SE polyoma virus; there were 9 survivors. As tumors became evident and/or after the tumor size impeded their activities, they were sacrificed. These mice showed positive alterations in the teeth and adjacent oral structures and all showed multiple tumors. A frequent site was the salivary glands. Many tumors were associated with the teeth, with invasion of the pulp chambers (directly through the base or by way of pulpal blood vessels). The pulp chamber's architecture was obliterated with tumor cells and the dentin was invaded from the pulp periphery. Hypertrophy of blood vessels caused destruction of pulpal elements and periodontium. Enamel formation was affected by invasion of tumor cells. There was marked proliferation of cementum, especially in the molar teeth.

- 64-75 THE VIRUS OF A ROUS SARCOMA INDUCING TUMOUR FORMATION AND HAEMORRHAGE IN CHICKENS AND HEN EMBRYO. (E.) Bamberger, K. (Veterin. Res. Inst. Hungarian Acad. Sci., Budapest). Acta Vet. Acad. Sci. Hung. 12(4):397-403, 1962.

A new strain of Rous sarcoma virus is described which often induces hemorrhage without tumor both in chick embryos and chickens. For inoc. a 10% suspension of tumor or of hemorrhagic, but tumor-free liver and spleen were employed. When inoc. onto the chorioallantoic membrane, focal or diffuse thickening of the membrane was observed; after i.v. inoc., only hemorrhages were observable. While tumors were not found in the embryos, the chicks that hatched showed the same pathological changes as the inoc. chickens. Among 440 chickens inoc. with tumor suspension (i.v. and i.m.) or hemorrhagic liver and spleen suspension (i.p., i.v. or i.m.), 99 developed tumors only, 129 only hemorrhages and 83 both tumors and hemorrhages; 129 were not affected.

4-76 VARIATIONS IN THE PATHOGENIC EFFECT OF MYELOID FOWL LEUKAEMIA VIRUS. (E.)

agerlöf, B. (Dept. Path., Karolinska Inst., Stockholm, Sweden) and P. Sundelin. Acta Path. Microbiol. Scand. 59(2):129-144, 1963.

Among groups of 135, 49, 51 and 18 White Leghorn chicks inoc. i.v. with 0.2 ml plasma from leukemic chicks infected with a myeloid strain of virus at 1-3, 4-7, 14 or 21 days of age, the incidence of classic myeloid leukemia was, resp., 4%, 49%, 33% and 12%. Incidence of subleukemic anemia, was, resp., 4%, 14%, 18% and 12%. In those inj. at the same times and observed at 60, visceral lymphomatosis developed in 3/7, 0/15, 1/16 and 5/13; kidney tumors developed in 1/7, 1/15, 2/16 and 5/13, resp. The kidney tumors were fixed and of the teratoid type.

4-77 THE PHYSICAL CHARACTERISTICS OF POLYOMA VIRUS. IV. THE SIZE OF THE DNA. (E.)

awford, L. V. (Inst. Virol., U. Glasgow, Scotland). Virology 22(1):149-152, 1964.

In a continuation of studies reported in CRA 1(2): 1964, 1963, the DNA of polyoma virus was examined by sedimentation velocity and equilibrium density gradient band-width measurement. Two velocity components were observed in the DNA preparations with sedimentation coefficients of 21S and 15.5S. The author suggests that the former coefficient represents the intact DNA of the virus (circular molecule with a molecular wt. of 3.5 million) and the latter coefficient results from the opening of the circular DNA. Equilibrium density gradient centrifugation in CsCl of the 21S component showed a band which was symmetrical and approx. Gaussian molecular wt. of approx. 2.5×10^6 . The equilibrium density gradient centrifugation showed the 15S component to have a symmetrical but not Gaussian band. This was probably due to the presence of two types of molecules of similar shape but of different densities. Density differences between the two types of slow component is approx. 0.01 g/ml.

-78 A SPECIFIC COMPLEMENT-FIXING ANTIGEN PRESENT IN SV40 TUMOR AND TRANSFORMED CELLS. (E.)

Black, P. H. (NIH, Bethesda), P. Rowe, H. C. Turner and R. J. Huebner. Proc. Nat. Acad. Sci. USA 50(6):1148-1156, 1963.

This paper presents evidence for a new, specific, complement-fixing (CF) antigen in SV40-induced tumors and transformed tissue culture cells (for preliminary description see CRA 1(9-10):#1740, 1964). Suspensions of hamster tumors (primary, transplanted and clone-induced) and cells of various species transformed by SV40 (hamster, rabbit, Swiss mouse, C3H mouse, pig) were shown to contain a specific antigen(s) when they were reacted with sera from hamsters bearing SV40 tumors. Although reaction occurred, antibody was not obtained in the same experiments with SV40

immune monkey serum was far lower. A low titer of antigen was also present in a suspension of second passage cells from a fetal bovine kidney culture chronically infected with SV40, but showing no evidence of transformation; the supernatant culture fluid at this passage level contained only small amounts of virus. This antigen has several properties which are distinct from the SV40 viral antigen(s): it is inactivated by heating at 50 or 56°C for 30 min. (SV40 viral antigen is unaffected); it is soluble, remaining unsedimented after centrifugation (SV40 viral antigen was completely sedimented after centrifugation); it has different serological reactivity. Antibody to the new antigen appears in hamster serum soon after the development of the tumor, and rises in titer as the tumors increase in size. CF antibody to viral antigen also developed, but usually much later and in lower titer than the neutralizing antibody. It seems evident that the new antigen is synthesized by information from SV40 viral genome integrated in the tumor and *in vitro* transformed cells.

64-79 SEARCH FOR VIRUS IN HUMAN MALIGNANCIES.

3. SEX SEGREGATION AND NEOPLASIA IN ICR/HA MICE. (E.) Girardi, A. J. (Merck Inst. Therap. Res., West Point, Pa.), M. R. Hilleman and R. E. Zwickey. Proc. Soc. Exp. Biol. Med. 114(3):609-614, 1964.

Mice of the ICR/Ha strain were sex-segregated and non-segregated at 21 days of age and were followed for development of neoplasia for a period of 650 days. In both groups of animals, the inj. of extracts of human malignant materials did not apparently influence the incidence of malignancy (mainly mammary carcinoma), which was in contrast to the findings of Grace. The death rate from non-neoplastic cause was roughly the same for sex-segregated and non sex-segregated groups. By contrast, the rate for occurrence of neoplasia was much higher among non-segregated animals; by day 400, 93 cases of neoplasia had developed among 1318 survivors of non-segregated mice (6.5%), whereas none of 158 surviving segregated animals had developed a tumor. The majority of neoplasms were mammary carcinomas and the second most frequent neoplasm was malignant lymphoma.

64-80 ELECTRON MICROSCOPIC OBSERVATIONS OF SIMIAN VIRUS-40 IN PRIMARY RHESUS KIDNEY TISSUE CULTURES. (E.)

Easton, J. M. (NIH, Bethesda). Proc. Soc. Exp. Biol. Med. 114(3):663-665, 1964.

SV40 particles were observed in monolayer cultures of infected rhesus kidney. The SV40 spread slowly through the cell sheet so that the virus particles were not visualized with the electron microscope until some time after infection. In contrast to results obtained with cercopithecus and erythrocebus monkey kidney, the SV40 particles appeared exclusively in the cell nuclei.

- 64-81 SIMIAN VIRUS 40 (SV-40): AN ONCOGENIC VIRUS. (E.) Eddy, B. E. (NIH, Bethesda). *Progr. Exp. Tumor Res.* 4:1-26, 1964.

This study is concerned with the history, properties, identification, preparation and preservation of Simian virus 40 (SV40) and its transmission to various animals. Thus far, SV40 has failed to induce known neoplasms or other illnesses in man and has not been shown to be oncogenic for its natural host, the monkey. Tumor response in newborn hamsters (1-3 days old) varied according to route of SV40 admin. (s.c., intracerebral, i.p., intrathoracic, in thigh bone, intranasal and p.o.). Hamsters older than 3 days and as old as 22 days (but not older) developed neoplasms after s.c. inoc. but required longer incubation periods than newborn animals. Of 3 adult *Cercopithecus* monkeys tested with 1 ml of SV40, one (s.c. route) died 17 days later and its infected organ cultures induced tumors when inj. into newborn hamsters. The 2 remaining monkeys (1 infected by the s.c., the other by the intracerebral route) are still under observation and after 17 mo. show no sign of disease. Newborn guinea pigs (hybrid, Hartley x NIH/F₁) and rabbits appear not to be susceptible. Of 31 NIH white mice given s.c. inoc. of SV40, 3 showed tumors. Of 10 Sprague-Dawley rats receiving s.c. inoc. of SV40 and surviving after 303 to 818 days, 3 developed tumors in the uterus and lung and 3 developed s.c. tumors.

- 64-82 SV-40 INDUCED PROLIFERATION OF TISSUE CULTURE CELLS OF RABBIT, MOUSE, AND PORCINE ORIGIN. (E.) Black, P. H. (Natl. Inst. Allergy Infect. Dis., Bethesda) and W. P. Rowe. *Proc. Soc. Exp. Biol. Med.* 114(3):721-727, 1964.

A proliferative response and cellular changes (epitheloid with an abnormal growth pattern) occurred in primary rabbit, mouse, and porcine kidney cultures infected with SV40 (0.1 ml of $10^{4.8}$ or $10^{5.3}$ TCID₅₀/0.1 ml) which resembled the transformations induced by the virus in hamster and human tissue culture. Continuous cell lines of the altered cells were established; preliminary attempts to transplant these cells to homologous or isologous species (rabbits and mice) have failed in contrast to previous work with transformed hamster cultures (see CRA 1(8):#1548, 1963). SV40 was not present as an extractable infectious virus in the passage lines of rabbit and mouse cells. (See also CRA 1(11):#1991 and *ibid.*, 1(12):#2157, 1964.)

- 64-83 MAMMARY CARCINOMA IN MICE BEARING A TRANSPLANTABLE MAMMOTROPIC TUMOR, CARRYING THE BITTNER VIRUS. (E.) Kunii, A. (Dept. Path., Francis Delafield Hosp., New York) and J. Furth. *Proc. Soc. Exp. Biol. Med.* 114(3):709-714, 1964.

Adult, virgin, female LAF₁ (C57/J x A/HeJ) mice,

in which spontaneous mammary tumors are very rare, showed the following mammary tumor (MT) incidence after transplantation with a subline of mammotropic tumor (MtT) strain 38 (used in previous cocarcinogenic studies with Bittner's virus): 4.5%, 31.0% and 71.4% in passages 3, 4 and 5, resp., with latency periods of 115-155 days. Numerous similar MtT strains studied earlier failed to induce mammary tumors. Electronmicrographs revealed the presence of Bittner mammary tumor virus (MTV)-like particles in both MT and mammary glands, indicating cocarcinogenic ties between MtT and MTV. No MT developed in bilaterally adrenalectomized mice bearing MtT but adrenalectomy enhanced the growth of the mammotropic tumor. The former effect may possibly be related to inhibition of milk secretion and reduction of viral conc. Cancerization by MtT strain 38 is unusual in that almost every mammary pad examined revealed microscopic mammary carcinomas (both glandular and squamous) and anaplastic (presumably precancerous) changes.

- 64-84 SARCOMAS IN COTTON RATS INOCULATED WITH ROUS VIRUS. (E.) Svet-Moldavsky, G. J. (Acad. Med. Sci., Moscow, USSR) and I. A. Svet-Moldavskaya. *Science* 143:54-55, 1964.

When newborn cotton rats (*Sigmodon hispidus hispidus*) were inoc. s.c. with Carr's strain of the Rous sarcoma virus (0.1-0.15 ml of a 30% homogenate of chicken Rous sarcoma), after survival for 2-3 mo., 12/23 developed sarcomas, some of which were solid and monomorphic with spindle shaped cells, while others exuded fluid when cut, showed a tendency to hemorrhage and rapidly became necrotic in the central parts. The significance of this sarcoma virus is discussed in relation to the pathogenicity of the various strains of this virus in other mammals.

- 64-85 ANALYSIS OF THE DEFECTIVENESS OF ROUS SARCOMA VIRUS, II. SPECIFICATION OF RSV ANTIGENICITY BY HELPER VIRUS. (E.) Hanafusa, H. (Virus Lab., U. California, Berkeley), T. Hanafusa and H. Rubin. *Proc. Nat. Acad. Sci. USA* 51(1):41-48, 1964.

In a continuation of earlier studies on the defectiveness of Rous sarcoma virus (RSV) reported in CRA 1(3):#506, 1963, disrupted non-producing (NP) cells (chick embryo cells infected with RSV but not producing mature RSV) failed to absorb measurable amounts of RSV neutralizing antibody from a Rous associated or helper virus (RAV). Inoc. of 2.7×10^2 or 2.7×10^3 NP cells into the wing webs of 2-week-old chicks induced visible tumors within 5 days; growth of the tumors continued for about 12 days, followed by regression periods in some animals, with some progression periods in others. Autopsy showed metastases in the lung and kidney. Six tumors were biopsied and showed cells with characteristic Rous sarcoma cell morphology, but no tumor produced virus

spontaneously, although every tumor retained the capacity for RSV activation by RAV. All chickens receiving NP cells developed tumors, but neutralizing antibodies to RSV were not detected at the highest conc. of serum (1:10) tested, while chickens infected with RAV alone developed neutralizing antibodies to RSV detectable at a 1:100 dilution of serum. In chickens bearing NP tumors there was a lack of immunity to RSV which was in sharp contrast to the high degree of immunity to RSV developed by the chickens as a result of infection with RAV and indicated that NP cells contain no RSV-specific coat antigens. RSV activated by different helpers was shown to have the same sensitivity to inactivation by absorbed antisera as its respective helper.

4-86 IN VITRO TRANSFORMATION OF CELLS OF RAT EMBRYOS INFECTED WITH CHICKEN SARCOMA VIRUS (BRYAN STRAIN). (Fr.) Rothschild, L. Dept. Cytobiol., Inst. Sci. Res. Cancer, Villejuif, Seine, France) and H. Febvre. C. R. Acad. Sci. (Paris) 257(22):3530-3532, 1963.

on infection of monolayered cell cultures of normal rat embryos with 1-10 PFU of Rous sarcoma virus (Bryan strain), the *in vitro* transformation of fibroblast-like cells into cancer cells was observed. Upon s.c. inoc. of these transformed cells (3-5 x 10⁵ cells, twice with 24-48 hr. intervals) into the dorsal region of newborn rats, malignant tumors developed at the inoc. site in 100% of the animals, whereas no tumors resulted from inoc. of uninfected cells or of medium from infected cultures. The above tumors grew successfully in 95-96% of the newborn or adult rats into which they were grafted. Cells from these newborn rat tumors, when directly inoc. into Leghorn chicks, provoked no tumor growth. If freshly trypsinized chick embryo cells were added to the newborn rat tumor cells, then typical Rous sarcoma tumors, containing the Rous virus, resulted after 2 wk. Similar results were obtained by previous irradiation (4,000 r) of the newborn rat tumor cells.

-87 ONCOGENIC EFFECT OF HUMAN ADENOVIRUS TYPE 12, IN MICE. (E.) Yabe, Y. Dept. Med., Baylor U., Houston, Tex.), L. Samper, Bryan, G. Taylor and J. J. Trentin. Science 163:46-47, 1964.

en newborn (less than 24 hr. old) mice, strains C3H/f/G_s, DBA/f, and A/f, were inj. with human adenovirus type 12 (strain Hu12) in equal doses (0.05 ml of infected tissue fluid) by the s.c., i.p., or intrapulmonary route, undifferentiated malignant tumors were induced at the site of the inj. in 4/13 C3H/f/G_s mice, but none were induced in DBA/f or A/f strains. The tumors were grossly and histologically similar to those induced by this virus in hamsters, but incidence was lower. Like the tumors in hamsters, the tumors in the mice were transplantable. In a subsequent group

of C3H/f/G_s mice, inj. i.p. with adenovirus type 12 at birth, 12/17 died of induced tumors in 56-155 days.

64-88 INFECTION WITH ADENOVIRUS TYPE 12. (E.) Pereira, M. S. (Virus Ref. Lab., Colindale, London) and F. O. MacCallum. Lancet 1:198-199, 1964.

In an 8-year-old boy with symptoms of meningitis, a specimen of feces taken 5 days after admission to a hospital was investigated in a series of tissue cultures (HeLa, human amnion and secondary monkey-kidney) susceptible to a variety of agents. Complement-fixation tests on the pt's. sera with antigens to poliovirus, mumps and herpes virus were negative. Only a strain of adenovirus type 12 was isolated which coincided with the child's illness. Newborn hamsters, when inoc. s.c. with 0.1 ml of undiluted tissue culture fluid from this strain, produced liver tumors and tumors (lymphosarcomas, in some places suggestive of reticulum cell sarcoma) at the inj. site. When extracts of the liver tumors were tested by complement-fixation, they were shown to react with an adenovirus type 12 rabbit antiserum, although long incub. of cultures of human embryo kidney inoc. with the extracts failed to show virus. In a serological survey of 455 sera (52 from normal infants aged 6 mo. to 1 yr., and 403 from age groups 1-50+ yr.), antibody to adenovirus type 12 was shown to be acquired early in life and is widespread in a high proportion of the population in England and Wales.

64-89 EFFECT OF A POSSIBLE ONCOGENIC VIRUS (ADENOVIRUS TYPE 12) ON LACTATE DEHYDROGENASE IN TISSUE CULTURE. (E.) Latner, A. L. (Roy. Victoria Infirmary, Newcastle/Tyne, England), P. S. Gardner, D. M. Turner and J. O. Brown. Lancet 1:197-198, 1964.

The effect of adenovirus 12 upon the distribution of 5 lactate-dehydrogenase isoenzymes was assayed in monkey-kidney cultures. The results were compared to those obtained for control monkey-kidney cultures and poliovirus infected monkey-kidney cultures. Adenovirus 12 after 6 days of culture produced a total lactate-dehydrogenase activity of 180 Berger-Broida U/ml of extract while poliovirus (PV) infected cultures produced approx. 130 U/ml and controls, approx. 135 U/ml. Adenovirus 12 infected material showed an isoenzyme pattern usually obtained with malignant tumors. It had a higher content of the more slowly moving isoenzyme component than the control or PV infected cultures. The fastest moving isoenzyme component (demonstrated in the control) was totally absent in the adenovirus infected culture. Human thyroid culture results with regard to total lactate-dehydrogenase and isoenzyme pattern were similar.

64-90 IN VITRO CULTIVATION OF MALIGNANT CELLS DERIVED FROM ADENOVIRUS-INDUCED HAMSTER

TUMORS. (E.) Strohl, W. A. (Dept. Microbiol., St. Louis U. Sch. Med., Missouri), H. C. Rouse and R. W. Schlesinger. Virology 21(3):513-516, 1963.

Cell cultures maintained for 9 mo. and derived from type 12 adenovirus-induced tumors were prepared from 2 sources: from animals with large s.c. tumors and from intrathoracic tumors in animals inoc. with a prototype strain of type 12 adenovirus. For purposes of comparison, cultures of adult, normal hamster lung were similarly established, but, unlike the tumor-derived cells, could not be maintained for more than 3 mo. Morphologically characteristic tumor-derived polygonal (HT) cells appeared in later, overcrowded, cultures. HT-culture cells showed a strikingly large number of cells recovered from fully grown plates: 6×10^7 cells/plate as compared with 4×10^6 cells/plate of normal hamster cultures. Karyotype analyses showed no tetraploidy. Metaphase figures of 32nd passage cells showed chromosome complements superficially similar to those of cultures of normal hamster cells. All cell lines retained their malignant properties *in vitro* for many generations: s.c. inoc. of 10^6 cells produced visible tumors within 10-15 days; inoc. with 10,000 cells developed tumors within 5 wk.; after inoc. of 100 cells, no tumors were seen in 20 wk. No tumors were observed after 18 wk. of observation with inoc. of 10^6 cultured normal hamster cells. Complement fixation tests on HT cell extracts demonstrated the persistence of viral specific antigens through the 25th passage *in vitro*. Sera of hamsters bearing tumors after inoc. of 10^4 HT cells (passage 9 or 12) contained complement-fixation antibodies reacting with type 12 virus-specific antigen and type 12 and 18 tumor extracts.

64-91 ELECTROPHORETIC PATTERNS OF PLASMA IN FOWL LEUKAEMIA. (E.) Lagerlöf, B. (Dept. Path., Karolinska Inst., Stockholm, Sweden) and P. Sundelin. Brit. J. Exp. Path. 44(6):621-624, 1963.

Comparative electrophoretic studies of plasma protein patterns in young (17-22 days) White Leghorn chicks with classic myeloid leukemia showed a significant increase in α -globulin levels ($0.05 > P > 0.01$) when compared to normal chick patterns, but no increase in γ -globulin fractions. Older leukemic chicks (59-168 days) showed reduced albumin fractions but significantly higher γ -globulin levels ($0.01 > P > 0.001$) than did young leukemic chicks. Young chicks (20-35 days) with subleukemic forms showed a significant increase of γ -globulins ($P < 0.001$), high α -globulin levels and a fairly high fibrinogen content (13-30%).

64-92 REDUCED ANTIBODY FORMING CAPACITY DURING THE INCUBATION PERIOD OF PASSAGE A LEUKEMIA IN C_3H MICE. (E.) Peterson, R. D. A. (Variety Club Heart Hosp., U. Minnesota,

Minneapolis), R. Hendrickson and R. A. Good. Proc. Soc. Exp. Biol. Med. 114(2):517-520, 1963.

A more detailed account of CRA 1(11):#1947, 1964.

64-93 FINE STRUCTURE OF A HUMAN BENIGN TUMOR VIRUS -- MOLLUSCUM CONTAGIOSUM VIRUS. (E.) Hung, T. (Dept. Virol., Chinese Acad. Med. Sci., Peking), L.-P. Ch'en and C.-F. 'P'ang. Chin. Med. J. 82(11):718-730, 1963.

As a result of electron microscope studies using chemical treatment and negative staining technics on the molluscum contagiosum virus, 4 kinds of particles (Type A, Type B, Type C and Type B-like particles) were observed. According to number, Type A particles were the most numerous, with Type C being the least frequent; in size, Type C was the largest with Type A the smallest. The surface structure of Type A particles shows wider and more numerous (by 4-5 stripes) crescentic stripes than does the orf virus, but clearer stripes than those of vaccinia virus. Widening and gradual disappearance of interstripe spaces after proteolytic enzyme (pepsin, trypsin) treatment was noted, and finally Type B-like particles were formed. The stripes eventually disappear and leave a thin sheet after persistent digestion; after digestion of Type B particles, no apparent effect was seen. Some dense bodies appear in Type A particles after combined action of proteolytic enzymes and nucleases. These bodies differ in shape and number when DNase and RNase are used separately. The hypothetical stereostructure of molluscum contagiosum virus is suggested and the morphologic relationship between the 3 main virus parts, stripes, nucleoids and dense bodies is also discussed.

64-94 ROUS SARCOMA IN HYDROCORTISONE-TREATED RATS. (E., Abstract) Ahlström, C. G., H. Grundsell and G. Sköld. Acta Path. Microbiol. Scand. 59(4):559, 1963.

Newborn rats were given hydrocortisone (H; 2.5 mg s.c.) and simultaneously inoc. with finely minced Rous chicken sarcoma in Hank's soln.; 1 wk. later a second dose was given. All H-treated rats developed s.c. tumors at the site of inoc.; almost all showed multiple tumors and the period of latency was shorter. Upon chromosome analysis, tumor cells showed rat-type chromosomes. In the control rats, 5/13 developed solitary tumors 40 days after inoc. No differences in takes or in the period of latency were seen in cortisone-treated newborn rats inj. with a cellular suspension or with an aliquot of homogenized material from the Rous chicken sarcoma. The effect of cortisone appears to be related to its capacity to inhibit antibody formation as well as to its antiphlogistic effect, permitting injected material to persist for a longer time.

64-95 STUDIES ON THE TRANSFORMATION OF HAMSTER EMBRYO CELLS IN CULTURE BY POLYOMA

VIRUS. I. PROPERTIES OF TRANSFORMED AND NORMAL CELLS. (E.) Stanners, C. P. (Dept. Biol., Massachusetts Inst. Tech., Cambridge), J. E. Till and L. Siminovitch. Virology 21(3):448-463, 1963.

A broad spectrum of inheritable, stable colony morphologies was found in 47 independent clonal isolates of cells obtained from polyoma virus infected hamster embryo cultures 10 wk. or more after infection. All produced rapidly growing neoplasms in 20-day-old hamsters. Many significant differences were reported when the cellular properties of 9 of the transformed clonal lines, believed to be representative of the entire morphological spectrum, were compared with the properties of freshly explanted hamster embryo cells. Transformed lines showed varied generation times, predominantly diploid metaphases, and the capacity for rapid production of extremely malignant, undifferentiated, spindle cell sarcomas with short latent periods.

4-96 STUDIES ON THE TRANSFORMATION OF HAMSTER EMBRYO CELLS IN CULTURE BY POLYOMA VIRUS. II. SELECTIVE TECHNIQUES FOR THE DETECTION OF TRANSFORMED CELLS. (E.) Stanners, C. P. (Dept. Biol., Massachusetts Inst. Tech., Cambridge). Virology 21(3):464-476, 1963.

Transformed cells could be detected at frequencies of 1 cell in 10^4 - 10^5 normal cells in reconstruction experiments where selective techniques were applied to artificial mixtures of small numbers of transformed cells and large numbers of normal cells. Cells of line Li, of particular interest because its cellular properties were closest to the properties of normal HA cells, could not be satisfactorily detected by any of these selective methods. The most successful technique for early detection entailed an initial period of growth of cells, plated immediately after adsorption of polyoma virus, in a selective liquid medium (1066 + 2% fetal calf serum) followed by application of a nonselective agar-liquid medium. New properties, such as a high relative plating efficiency in media containing low conc. of serum, on which the techniques depend, seem to be conferred upon cells very soon after infection with virus.

4-97 STUDIES ON THE S.E. POLYOMA VIRUS. THE CYTOPATHOLOGIC EFFECT, THE INFECTION AND HEMAGGLUTININ TITERS IN MOUSE EMBRYONIC CELLS. A COMPARISON OF CELLS FROM DIFFERENT STRAINS. (It.) Jemolo, A. M. (Dept. Microbiol., Superior Institute Health, Rome) and G. Castelli. Rendic. Ist. Sup. Sanit. 26(1-2):1-90, 1963.

E polyoma virus 210-877/4 was inoc. (10 to 100,000 TCID) into trypsinized tissue cultures of embryonic cells from mice of the following strains: A/Yax, C57BL/6, PRI, Swiss/Webster/Ar,

C57BR, and Swiss/ISS. Highest single hemagglutinin titers (640 for 10 TCID; 1280 for 100,000 TCID) and greatest cytopathologic effect and hemagglutinin titer after 14 days (10^8 and 10^7 , resp.) were found in C57BL/6 embryonic cells, which makes this the most suitable strain for growing this virus.

64-98 A NEW STRAIN OF ASCITES LEUKEMIA IN MICE. (E.) Shirasu, Y. (Inst. Phys. Chem. Res., Tokyo, Japan) and C. Itakura. Gann (Jap. J. Cancer Res.) 54(4):501-502, 1963.

Small pieces of tumor tissue (enlarged submaxillary lymph node) from a 12-month-old ddOM female mouse with spontaneous lymphatic leukemia were successfully transplanted into 10 mice of the same strain. When s.c. tumor tissue from passage two was inoc. i.p. into mice of the same strain, enlargement of the abdomen with retention of leukemic ascites in all of the mice occurred within 2 wk. The ascites tumor cells were maintained for more than 60 passages and were designated as ascites leukemia SR-61; survival of tumor bearing mice ranged from 2-4 wk. Negative results were obtained from transplantation of ascites leukemia SR-61 into other dd strains. When the ascites tumor cells were inj. s.c., tumors (s.c.) weighing about 4 g were formed. The SR-61 ascites tumor cells showed a slightly higher susceptibility to anticancer chemicals in preliminary testing (no further details).

64-99 NEW PAPOVAVIRUS CONTAMINATING SHOPE PAPILOMATA. (E.) Hartley, J. W. (NIH, Bethesda) and W. P. Rowe. Science 143:258-260, 1964.

A virus, tentatively designated as the rabbit kidney vacuolating (RKV) virus, was isolated from several naturally occurring cottontail (Sylvilagus sp.) papillomata. The virus produced cytopathic effects rapidly (3-5 days) and to the greatest extent in domestic rabbit kidney cultures in Eagle's basal medium. Plaques of 0.5-1 mm in diameter were seen after 11 days in rabbit kidney cultures overlaid with agar. The physical and chemical properties, cytopathic effects, hemagglutination characteristics, and electron microscope findings seem to indicate that RKV is not Shope papilloma virus, but a previously undescribed nonpathogenic agent related to the papovavirus group.

64-100 VIRUS-LIKE PARTICLES IN HUMAN CHLORO-LEUKEMIA CELLS. (E.) Ota, Z. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Suzuki and S. Higashi. Gann (Jap. J. Cancer Res.) 54(4):481-486, 1963.

Presentation in English of a paper abstracted as CRA 1(12):#2154, 1964.

See also abstract no.: 3

EPIDEMIOLOGY AND BIOMETRY

- 64-101 A CANADIAN STUDY OF SMOKING AND HEALTH--
SECOND REPORT. (E.) Best, E. W. R.
(Div. Epidemiol., Dept. Natl. Health Welfare,
Ottawa, Ont., Canada) and C. B. Walker. Canad.
J. Public Health 55(1):1-11, 1964.

Results of a study are presented, mainly of 77,922 male pensioners (World Wars I, II and Korean War) but excluding those hospitalized, made between July 1956 and June 1962. Comparison of age-specific death rates for all causes of death combined show that for males age 30 and over, the excess observed deaths over the expected number for non-smokers for all who smoked cigarettes only was 52%.

- 64-102 RECONSIDERATION OF SOME SIGNIFICANT
ASPECTS OF THE CIGARETTE SMOKING--LUNG
CANCER CONTROVERSY. (E.) Delarue, N. C. (Dept.
Surg., Toronto Gen. Hosp., Canada). Canad. Med.
Assn. J. 89(25):1277-1283, 1963.

Common questions concerning smoking and the relationship to lung cancer are answered and discussed with emphasis on the biological features in human oncogenesis, experimental oncogenesis and the role of carcinogens and cocarcinogens. Influences causing the delay in acceptance of the association between cigarette smoking and lung cancer are attributed to wrongly conceived doubts concerning epidemiological evidence, lack of proper leadership incentive, advertising, overemphasis on the influence of addiction, and genetic variation. It is concluded that the complex relationship between carcinogens and cocarcinogens makes the development of a safe cigarette unlikely; hence, if therapy cannot be dramatically improved, means to curtail smoking should be undertaken.

- 64-103 SURGERY FOR CARCINOMA OF THE ESOPHAGUS
AND THE CARDIA. REVIEW OF 105 CASES.
(E.) Johansson, L. (Dept. Thorac. Surg.,
Karolinska Inst., Stockholm, Sweden), T. Silander
and S. Söderlund. Ann. Chir. Gynec. Fenn. 52(4):
429-436, 1963.

In the series of 105 cases reviewed, the ratio (male, female) was about 5:1 (88 and 17, resp.). The youngest pt. was age 37 and over one-half were aged 55-65. In the present series, 54 pts. (53 men, 1 woman) used spirituous liquors in varying amounts and 55 pts. (53 men, 2 women) were smokers; 48 men were both smokers and used alcohol.

- 64-104 CHROMOSOME DELETION IN A CASE OF RETINO-
BLASTOMA. (E.) Lele, K. P. (St.
Bartholomew's Hosp., London), L. S. Penrose and
H. B. Stallard. Ann. Hum. Genet. 27(2):171-174,
1963.

In the course of an investigation of the karyotypes

of pts. with retinoblastoma, among 6 examined, 1 was found in whom all cells showed a deletion in the longer arm of one of the large acrocentric chromosomes. The other pts. had normal karyotypes.

- 64-105 PELVIC CANCER IN CINCINNATI. A 5-YEAR
STUDY. (E.) Cole, S. (Dept. Obstet.
Gynec., Bethesda Hosp., Cincinnati, Ohio). Obstet.
Gynec. 23(2):274-278, 1964.

Between 1957-61, 1249 female pelvic cancer pts. were seen in Greater Cincinnati hospitals. Average age according to type of malignancy was: invasive squamous cervix 525 pts., 51.2 yr.; adenocarcinoma corpus 384 pts., 60.2 yr.; carcinoma vulva 34 pts., 61.8 yr.; invasive cervical adenocarcinoma 20 pts., 55.0 yr.; carcinoma of the vagina 10 pts., 70.2 yr.; carcinoma of the uterine tube 4 pts., 74.0 yr. In 1500 pts. 1509 cancers were found. The annual incidence (per 100,000) for all women with cervical malignancy was 29.7 (White 26.4, Negro 49.4, Jewish 2.7). White or non-White, the higher the socioeconomic status, the lower was the incidence of cervical malignancies. The ratio of cervical to corporeal cancer for all pts. was 1.8:1 (White 1.6:1, Negro 4.6:1), of adenocanthoma of the corpus to adenocarcinoma of the corpus, 1:20. Among 18 pts. with 2 or more primary malignancies, 9 were multiple cancers of the genital system.

- 64-106 BRONCHOGENIC CARCINOMA: RELATION TO
ANTECEDENT PULMONARY INFECTION. (E.)
Rosenblatt, M. B. (New York Med. Coll., N. Y.)
and M. Yildiz. Dis. Chest 44(6):598-601, 1963.

Between 1951-1960, 253 pts. with bronchogenic carcinoma were seen at the Metropolitan Hospital, N. Y. Sex distribution was 210 men and 43 women; age distribution was similar for both sexes with most cases occurring in the 6th, 7th and 8th decades. There was a history of previous pulmonary infection of 5 or more yr. duration in 102 (40%) cases: influenza 12 (11.7%), bronchitis 10 (9.8%), pleurisy 6 (5.9%), pneumonia 52 (50.9%) and tuberculosis 22 (21.7%). With respect to anatomic distribution of tumors or histologic differentiation, there were no striking differences between 102 cases with infection and 151 cases without infection. Among the exceptions were 2/7 cases of alveolar carcinoma which occurred in the non-infection group; the remaining 5 had a history of pneumonia.

- 64-107 BIOLOGICAL STUDIES ON THE NEW ALBINO
MOUSE INBRED AT THE INDIAN CANCER RE-
SEARCH CENTRE. (E.) Ranadive, K. J. (Dept. Appl.
Biol., Indian Cancer Res. Ctr., Bombay) and S. A.
Kanekar. Indian J. Med. Res. 51(6):1005-1014, 1963.

A study was made of incidence of spontaneous breast

tumors in I.C.R.C. mice from generations F_6 to F_9 . In female virgin mice 6-8 mo. of age, incidence was 3/15 (20%); in the 10-12 mo. group, 3/12 (25%) with multiple tumors; in those over 1 yr., 7/18 (88%) (5 multiple). In breeding females of the groups 6-8 mo., 8-12 mo. and over 1 yr., number with breast tumors was, resp., 5/8, 20/22 and 11; 7/34 tumor-bearing animals had multiple breast tumors. The morphology of mammary glands and the histology of ovaries, adrenals, uterus and pituitary was also studied at different age periods. The histological structure of the ovaries and adrenals indicated hyperactivity at an early age which evidently influenced the fast growth of target organs and the early development of precancerous lesions.

-108 VITAL STATISTICS OF THE UNITED STATES, 1961. VOL. 2 - MORTALITY. PART A. Under, F. E. (Director; Natl. Ctr. Health Statistics, Washington, D. C.). U. S. Dept. Health, Educ., Welfare. U. S. Govt. Print. Office, Washington, D. C., 1964. \$3.75.

Compilation of mortality rates of the population in the USA, for 1961, for various diseases, including malignant neoplasms, in relation to sex, age, race and geographic location by state. Data are given on mortality rates for malignant neoplasms of various organs for the individual years between 1951 and 1961.

-109 VITAL STATISTICS OF THE UNITED STATES, 1961. VOL. 2 - MORTALITY. PART B. U. S. Dept. Health, Educ., Welfare. Public Health Serv. Natl. Vital Statistics Div. U. S. Govt. Print. Office, Washington, D. C., 20402. 7 pp., 1963. \$4.50.

Compilation of mortality statistics for the year 1961, including those on malignant neoplasms, classified with respect to site, as well as age, color and sex of pt., for the various states of the United States and certain urban and rural areas. Data on Puerto Rico and the Virgin Islands are also included.

-110 VITAL STATISTICS OF THE UNITED STATES, 1962. VOL. 2 - MORTALITY. PART A. Under, F. E. (Director; Natl. Ctr. Health Statistics, Washington, D. C.). U. S. Dept. Health, Educ., Welfare. U. S. Govt. Print. Office, Washington, D. C., 1964. \$3.75.

Compilation of mortality data for 1962 on deaths in the USA from various causes, including malignant neoplasms in various, specified organ systems, in relation to color, sex, age and geographic location by state.

-111 VITAL STATISTICS OF THE UNITED STATES, 1962. VOL. 2 - MORTALITY. Part B.

U. S. Dept. Health, Educ., Welfare. Public Health Serv. Natl. Vital Statistics Div. U. S. Govt. Print. Office, Washington, D. C., 20402. 563 pp., 1964. \$4.50.

A compilation of mortality statistics for the year 1962, including those on malignant neoplasms, classified with respect to site, as well as age, color and sex of pt., for the various states of the United States and certain urban and rural areas. Data on Puerto Rico and the Virgin Islands are also included.

64-112 CANCER MORTALITY IN FRANCE. (Fr.) Girond, J. Sem. Med. Prof. 40(4):67-68, 1964.

Cancer deaths per 100,000 in France for 1960 and 1961 were, resp.: for the population as a whole, 198 and 199; males, 213 and 218; females, 183 and 181. Compared to deaths from all causes, male cancer deaths represented 19.5 and 20.7%, resp.; for females, 18.6 and 19.2%. For both sexes, a progressive (but not constant) increase has been evidenced ever since 1951, when male cancer deaths represented 14.4% of all male mortalities and female cancer deaths represented 15.2% of all female mortalities. During the same period, 1951-1961, the major increases (percentage) of male mortality from cancers of specific sites have been: lungs, bronchi and trachea, 100; prostate, >40; leukemias, >50; buccal cavity and pharynx, >55; lymphosarcoma and related disorders, >40; esophagus, 25; breast, >20. The major decreases (percentage) have been: bone and connective tissue, >10; stomach, 15; skin, 30. The major increases (percentage) among females have been: leukemias, >55; buccal cavity and pharynx, 35; lymphosarcoma and related disorders, 25; cervix uteri, 30; esophagus, 35; breast 10. The major decreases (percentage) have been: bone and connective tissue, 10; larynx, 20; uterus (site not specified), 15; stomach, 20; and skin, 15.

64-113 THE ACTION OF TUMORIGENIC TREATMENTS AND PROTECTIVE AGENTS ON MELANOTIC TUMOR FORMATION IN *D. MELANOGASTER*. (E., Abstract) Burnet, B. (A.R.C. Poultry Res. Ctr., Edinburgh, Scotland). Heredity 18(Pt. 4):554, 1963.

In the *tu bw:st su-tu* strain of *Drosophila melanogaster*, which carries a melanotic tumor gene on the second chromosome and a specific tumor suppressor on the third chromosome, studies on the protective effect of l-cysteine, l-methionine and cystamine indicates that the increased tumor penetrance caused by X-ray treatments or excess of l-tryptophan in the diet occurs through a genetically controlled defect of sulfur metabolism and not through action on the tryptophan peroxidase-oxidase mediated reaction as suggested by Plaine and Glass. (See also CRA 2(1):#114, 1964.)

- 64-114 EFFECTS OF ENVIRONMENTAL MANIPULATION ON THE PENETRANCE OF MELANOTIC TUMOURS IN SUPPRESSED AND UNSUPPRESSED STRAINS OF D. MELANOGASTER. (E., Abstract) Sang, J. H. (A.R.C. Poultry Res. Ctr., Edinburgh, Scotland). Heredity 18(Pt. 4):554-555, 1963.

Tests with germfree synthetic diets containing excesses or deficiencies of individual nutrients showed that the tumor penetrance of the strain *tu bw:st su-tu* was affected in the same way also in the presence or absence of the *su-tu* suppressor gene. Thus the treatments influence the expression of the tumor gene directly, rather than through the suppressor gene. Since many metabolically unrelated treatments are similarly effective, it is unlikely that they operate directly through a specific metabolic pathway. (See also CRA 1(3):#406, 1963 and *ibid.*, 2(1):#113, 1964.)

- 64-115 PHYSIOLOGICAL GENETICS OF MELANOTIC TUMORS IN DROSOPHILA MELANOGASTER. I. THE EFFECTS OF NUTRIENT BALANCE OF TUMOR PENETRANCE IN THE *tuK* STRAIN. (E.) Sang, J. H. (Agricul. Res. Council Poultry Res. Ctr., Edinburgh, Scotland) and B. Burnet. Genetics 48(1):235-253, 1963.

Omission of RNA from a germfree, chemically defined medium resulted in the induction of melanotic tumors in 70.4% of the individuals of *tuK* strain of Drosophila melanogaster, compared to an incidence of 1.6% in the controls, growing in a medium containing 0.4% RNA. Low cholesterol content of the medium (0.00156%) caused tumors in 75% of the flies and, when combined with reduced RNA (0.1%), in 90%. Normal cholesterol level was 0.03%. These two deficiencies are independent since an excess of RNA does not counteract the deficiency of cholesterol or vice versa. A study of the effect of pentose and deoxypentose nucleotides showed that the RNA requirement for tumor suppression was specifically for the nucleotide or nucleoside of adenine and also that there is an antagonistic interaction between dietary levels of adenylic and cytidylic acid. The effect of RNA deficiency on tumor penetrance is enhanced by deficiencies of folic acid, pyridoxine, thiamine and biotin. Changing the conc. of adenylic and cytidylic acid in the diet at certain times in development showed that the *tuK* gene acts at the time of molting at the end of the second larval stage. Melanization of tumors is controlled by the pupation hormone and is thought to coincide with an alteration of the redox potential of the hemolymph which releases an inhibition of the enzyme tyrosinase. (See also CRA 2(1):#114, 1964.)

- 64-116 THE PROBLEM OF MALIGNANCY IN NODULAR GOITER. (Sp.) Litvak, J. (Dept. Med., U. Chile Sch. Med., Santiago), O. Lopez, I. Zanzi, M. Barahona, J. Kappes and L. Figueroa. Rev. Med. Chile 91(9):631-634, 1963.

In Chile (provinces of Coquimbo, Santiago, Linares and Nuble), nodular goiters were found in 16.6% of all school children examined, 14.0% of pts. hospitalized for other causes, and 25.0-28.7% of pts. autopsied in contrast to an estimated, maximal incidence of 28 cases of thyroid cancer per 1,000,000 inhabitants per yr. Among Chileans with nodular goiters, the estimated (maximal) incidence of thyroid cancer was 0.02%.

- 64-117 NOTES ON THE EPIDEMIOLOGY OF PULMONARY CANCER. (Por.) Teixeira, J. (Dept. Surg. Grad. Sch. Med., Catholic Pontifical U., Rio de Janeiro, Brazil). Rev. Brasil. Med. 20(8):451-453, 1963.

In a general review (8 references) of statistics concerning the incidence of bronchogenic cancers, the author reports that the incidence of malignancies (percentage) shown at autopsy in the city of Rio de Janeiro between 1919-27, 1919-43, 1943-53, and 1950-61 was 6.9, 8.6, 15.4, and 10.2, resp. For these same periods, incidence (percentage) of malignancies which were primary pulmonary neoplasms was 2.8, 4.5, 8.6, and 16.0, resp. In 1940, the mortality rate (per 100,000) for cancers of the respiratory tract was 2.0; in 1960, it was 10.2, with a significantly greater part of the increase being seen among men.

- 64-118 THE CYTOLOGY AND CYTOCHEMISTRY OF ACUTE LEUKAEMIAS. A STUDY OF 140 CASES. (E.) Hayhoe, F. G. J., D. Quaglini and R. Doll. Privy Council. Med. Res., Council Spec. Rpt. Ser. No. 304. London, Her Majesty's Sta. Off. (Univ. Dec. Classif. 616.155.392-091.8), 105 pp., 74 plates, London, 1964.

A detailed cytological and cytochemical study is presented of 140 consecutive cases of acute leukemia. Included are 74 illustrations in color and a bibliography with 108 references. After an analysis of the data a correlation was made with various biological characteristics of the subgroups: relation of type to age and sex and duration of disease. The data provide additional evidence that lymphoblastic cases differ in nature from the others. After a discussion of the cytochemical patterns and a detailed consideration of each cytochemical reaction, arguments are put forward that the cytochemical appearances in leukemic cells are consistent with a prolongation of interphase, resulting in a low rate of proliferation and asynchronous nuclear-cytoplasmic development.

- 64-119 ATMOSPHERIC POLLUTANTS. (E.) WHO Expert Comm. Atmospheric Pollutants. WHO Techn. Rep. Ser. #271:3-16, 1964.

This report by an international group of experts reviews progress in air pollution control and then focuses attention on problems of international interest (motor vehicle exhausts, elimination of SO₂

from flue gases, adequate and timely assessment of meteorological factors, studies of morbidity associated with air pollution and the development of methods of utilizing poor quality coal with a minimum of air pollution. Recommendations are made relative to standardization of nomenclature, units and methods of measurement and criteria and guides are offered for evaluation of air quality.

120 WHO EPIDEMIOLOGICAL AND VITAL STATISTICS REPORT. (E.) Epidem. Vital. Statist. Rep. 17:113-152, 1964.

This report deals with the 10 leading causes of death (including neoplasms) for selected countries in Africa, South and Central Africa and Asia for 1954-56, 1960 and 1961.

121 EPIDEMIOLOGICAL AND VITAL STATISTICS REPORT. (E. and Fr.) WHO (Geneva) 11-2:1-112, 1964.

Part II of this report gives the 10 leading causes of death during 1954-56, 1960 and 1961 for Canada, USA, Austria, Belgium, Denmark, France, Federal Republic of Germany, West Berlin, Hungary, Ireland, Italy, The Netherlands, Norway, Portugal, Sweden, Switzerland, United Kingdom (England and Wales, Scotland, Northern Ireland), Australia and New Zealand. For all ages, ages 1-4, 5-14, 15-44, 45-64, and 65 and over are given the number of deaths, death rates and the percentage of each cause to total causes for the period indicated. In 1961 deaths from malignant neoplasms occupied second place in all countries except West Berlin where they ranked third (rate 329.9, 20.3% of all deaths); Italy, third (148.4 and 16.0%); and Portugal, fifth (97.4 and 9.0%).

122 VITAL STATISTICS FOR 1962. PROVINCE OF ONTARIO. (E.) Yaremko, J. 93rd Annual Statistics Rept. Off. Registrar General. Toronto, F., Queen's Printer, 221 pp., 1964.

This report of vital statistics for the Province of Ontario includes deaths from neoplasms; among the tabulations are deaths by site and county; Toronto by sex and age; and by site in cities and towns over 5,000 (recorded according to county).

123 MALIGNANT TUMORS OF THE NASOPHARYNX. (Rus.) Tran Hu Tuok (Clin. Otorhinolaryng., Fac. Med., Hanoi, N. Vietnam), Le Van Loi, Tran, Fam Kim and Le Si Nhon. Vest. Otorinolaryng. 25(6):41-44, 1963.

During a 6-year period (1955-1961) the authors diagnosed 369 malignant tumors of the nasopharynx in N. Vietnam. Among 70 of these pts. (46

male, 24 female) between the ages of 15-65 who were studied in detail, there were 46 epitheliomas (2 basal cell, 26 spinocellular, 3 intermediate, 1 mixed, 14 atypical) and 24 sarcomas (8 lympho-, 13 reticular cell, 2 histiocytic, 1 fibro-). These cases were grouped and discussed according to early signs as follows: 44 hemorrhagic; 70 aural (otorrhea, loss of hearing, tinnitus); 38 nasal (obstruction, excessive nasal discharge, hyposmia or anosmia); ganglionic, mainly metastatic (enlargement of cervical lymph nodes in 28, multilocal enlargement in 46); 44 neurologic (neuralgic headaches, paralysis of the cranial nerves and Horner's syndrome).

64-124 MALIGNANT NEOPLASMS IN PLZEN IN THE YEARS 1957-1958. (ANALYSIS OF INCIDENCE, PREVALENCE, MORBIDITY, AND MORTALITY). (Cz.) Zaremba, V. (Charles U., Prague). Plzen. Lek. Sborn. 18:79-99, 1963.

Age incidence of new malignancies within the 2-yr. period among 453 men and 485 women was, resp.: up to age 19, 5 and 2; 20-49 yr., 53 and 104; 50-64 yr., 218 and 195; above 65 yr., 177 and 182; age unknown, 0 and 2. The most frequent tumor sites were: in men, lungs 95 (21.0%); skin 55 (12.2%); stomach 54 (11.9%). The most frequent sites in women were: uterus 115 (23.9%); breast 83 (17.2%); skin 62 (12.9%); stomach 54 (11.2%). During the 2-yr. period, mortality (men, women) in pts. at age below 50 yr. was, resp.: 17.7% and 21.7%; at age below 65 yr. it was 29.2% and 32.9%; overall mortality (all age groups) was 26.4% and 23.1%. Mortality was 29.8% in lung cancer of men; 16.2% in stomach cancer of men; 14.6% in stomach cancer of women; 14.6% in mammary cancer of women; and 10.5% in uterine cancer. Incidence, prevalence and mortality of various primary cancer sites in men and women are presented diagrammatically.

64-125 THE RELATION OF BLOOD GROUPS A, B, O, AND AB AND THE RH FACTOR TO THE INCIDENCE OF SALIVARY GLAND TUMORS. (E.) Dunkel, J. C. Northwest. Univ. Bull. 63(35):15-18, 1964.

In 100 salivary gland tumor pts. from the Chicago area, distribution according to blood groups was: A, 44.7%; B, 16.1%; O, 37.5%; AB, 1.8%; Rh-, 17.5%. No significant differences were found when compared to normal populations.

64-126 CANCERS OF THE MOUTH. (Fr.) Jaumet, E. (Cancer Inst., U. Louvain, Belgium), J. Maisin and C. Deckers. J. Radiol. Electr. 44(11):727-734, 1963.

In a review (30 references) of the etiology, symptomatology, classification and treatment of oral cancers (excluding cancers of the tongue), the authors present an analysis of 148/155 original cases seen at a mean age of 61.74 yr. (range, 28-82 yr.) for men and 64.5 yr. for women. Males

comprised 84% of the pt. group. All cases seen involved spinocellular or epidermoid carcinomas (although the authors report having also seen pts. with epulis, mixed tumors, myeloplax, plasmacytomas, cylindromas, and spindle cell sarcomas). A majority of these pts. were or had been smokers. Stumps of teeth or poorly fitting dentures, which provoked chronic mucosal irritation, were frequently seen. One cancer was developed from a syphilitic lesion; positive Bordet-Wassermanns were obtained in 3/18 pts. tested. In 8/27 female pts. included in a fragmentary study, cancers developed from leukoplakia. The authors report that oropharyngeal cancers account for 1.1% of all reported neoplasms in Belgium.

- 64-127 CEREBRAL TUMORS IN AFRICANS. (REPORT OF 43 CASES.) (Fr.) Collomb, H., B. Courson, Y. Philippe, A. Carayon, R. Camain and M. Dumas. *Bull. Soc. Med. Afr. Noire Lang. Franc.* 8(3):261-278, 1963.

The neuropsychiatric service of a Dakar hospital reports finding 37 cerebral malignancies and 6 cerebral tuberculomas during the 4 yr. preceding report. The malignancies included 13 meningiomas, 12 gliomas, 2 astrocytomas, 2 pituitary tumors, 1 medulloblastoma, 1 craniopharyngioma, 5 metastases, and 1 unclassified tumor of the sellar region. While sex and ethnical origin bore no relationship to the incidence of tumor types, age appeared to be a significant factor. Supratentorial gliomas occurred preferentially in subjects older than 48 yr.; meningiomas developed earlier between 35-40 yr. of age (range of 18-54). Metastatic tumors involved 40-60-year-old pts. except in the case of a 24-year-old man. The authors conclude that the incidence of these disorders among the native population of Africa is probably comparable to that in Europe; and that previous reports of their rarity were due to inadequate facilities for hospitalization and/or observation.

- 64-128 SIMULTANEOUS OBSERVATION IN BLADDER DIVERTICULUM OF SARCOMA, CARCINOMA AND STONES. (Hun.) Kelenhegyi, M. (1st Clin. Surg., Debrecen U. Sch. Med., Hungary), J. T. Kelemen and G. Horváth. *Magy. Sebesz.* 16(2):138-141, 1963.

A rare case is presented of a 68-year-old man with simultaneous sarcoma and a separate carcinoma arising in a bladder diverticulum. The tumors are believed to be related to the chronic irritation from bladder stones and difficulties in voiding urine.

- 64-129 THE USE OF STATISTICS IN THE ETIOLOGICAL STUDY OF MALIGNANT NEOPLASMS. (E.) Clemmesen, J. (Dept. Path., Finsen Inst., Copenhagen, Denmark). *Internat. Rev. Exp. Pathol.* 2:139-197, 1963.

The history, principles and application of methods used in the statistical study of cancer are reviewed (approx. 150 references) and evaluated. Emphasis is placed on the limitations and shortcomings of prevalence, ratio, rate, and demographic studies. Individual interview is considered to be the best method of investigation. Rate studies are preferable to ratio studies since the latter are affected by accidental changes in general mortality, the independent rise in frequency of a single neoplasm, the age difference in primitive young populations compared to older industrialized ones; prospective studies should be carried out on the basis of registration of cases to provide the answer to the relative risks of certain types of cancer in relation to certain suspected carcinogens. It is concluded that the most useful studies may be of persons with a particular neoplasm studied along with a corresponding number of control persons selected with a view to the applicability of a single suspected carcinogen; such studies should be made with close cooperation of statisticians, pathologists and investigators (clinical and experimental).

- 64-130 MYCOSIS FUNGOIDES IN A FAMILY OF PSORIATICS. (E.) Aguilera Maruri, C. (Valdecilla Clin., Santander, Spain). *Skin* 3(1):10-12, 1964.

This paper contributes an interesting case report on the much discussed relationship of psoriasis and psoriasiform conditions to mycosis fungoides. The pt., age 57, female, presented with skin lesions of 2 mo. duration in the dorsolumbar areas and abdominal wall, with all the clinical characteristics of parapsoriasis en plaques. The histologic appearance corresponds to an erythematous plaque of mycosis fungoides. In her family history, psoriasis was found in an older sister and in another now dead of heart disease. The only daughter of the pt., now age 30 and in her 7th mo. of pregnancy, suffers from pruritus but without lesions.

- 64-131 AN APPROACHING METHOD FOR FINDING CAUSATIVE AGENTS OF HUMAN CANCERS OF ENVIRONMENTAL ORIGIN THROUGH THE ANALYSIS OF THE RELATION BETWEEN THE DISTRIBUTION OF THE AGENTS AND THE INCIDENCE RATES OF THE CANCERS, WITH APPLICATIONS TO OESOPHAGUS AND GASTRIC CANCERS. (E.) Sato, T. (Dept. Nutr. Biochem., Inst. Public Health, Tokyo, Japan). *Bull. Inst. Public Health* 12(3):160-165, 1963.

The author analyzes a method for finding causative agents of human cancers in relation to the canceration rate (cancers among deaths influenced by the cause), life span and incidence rate. This testing method has been applied to esophagus and gastric cancers. Cancer of the esophagus in Japan, France, Switzerland, Thailand and South Africa has been associated with hot foods and drinks, and in some pts., the anesthetic effect

of alcohol has enabled them to swallow hot foods unconsciously. Gastric cancer in Japan, North Wales, slums of Oslo, Finland, Seeland of The Netherlands, Austria and occidental Jews has been associated with the swallowing of highly salted foods without sufficient mastication. Repeated hemorrhages in the stomach wall are explained by high osmotic pressure of the salt confined in the food stuffs. Prolonged admin. of salt tablets to a rabbit (1 g 1-2x/wk. for 2.5 yr.) caused a stomach tumor. Solid foods of 3% brine conc. caused hemorrhage in the stomach membrane of experimental animals.

64-132 BOWEN'S DISEASE AND ITS RELATIONSHIP TO SYSTEMIC CANCER. (E., Abstract) Graham, J. H. (Armed Forces Inst. Path., Washington, D. C.) and E. B. Helwig. Pp. 1599-1601 in *Proceed. XII Internatl. Congress Dermatology. Sept. 1962. Washington, D. C. Vol. II.* Pillsbury, D. M. and C. S. Livingood (Eds.). Excerpta Medica Found. Internatl. Congress Series 55, Amsterdam, 1652 pp., 1963.

Further discussion is presented of the association of Bowen's disease of the skin with systemic and cutaneous cancer (see CRA 1(3):#380, 1963). The involved sites, in order of frequency were: skin, respiratory tract, gastrointestinal tract, genitourinary organs, RES, oral cavity, extracutaneous sites (soft tissue of the neck, mucous membrane of lip and eye), breast, and endocrine system. Heredity or the predisposition to the development of cancer was suggested by the occurrence of internal cancer in 1 or more members in 37/77 (48%) families.

64-133 PERSONALITY AND LUNG CANCER. (E.) Kissen, D. M. (South. Gen. Hosp., Glasgow, Scotland). *Lancet* 1:216-217, 1964.

Further observations are reported on the paper abstracted as CRA 1(3):#535, 1963. The personality features described as poor outlet for emotional discharge were present even when cigarette smoking was held constant, just as cigarette smoking was a dominant feature when personality was held constant. However, if one takes into account degree of exposure of bronchi to cigarette smoke (which acknowledges inhaling habits), the findings suggest that the poorer the outlet for emotional discharge the less the exposure to cigarette smoke required to induce lung cancer. Thus in a series of 214 lung cancer pts. graded in 5 grades of descending order of exposure to cigarette smoke (including non-smokers) the mean neuroticism scores were 4.0, 3.8, 3.5, 2.2, 2.0.

64-134 DESMOID TUMOURS. A SERIES OF 33 CASES. (E.) Dahn, I. (Dept. Surg., U. Lund, Sweden), N. Jonsson and G. Lundh. *Acta Chir. Scand.* 126(4):305-314, 1963.

All 33 cases of desmoid tumor, representing an estimated incidence of 2/yr./million people, were seen in the course of 15 yr. at the Institute of Pathology, Lund. There were 28 women (26 of child-bearing age) and 5 males (4 between 30-50 yr.). A history of childbirth or abdominal surgery existed in 23/33, in 10 cases less than 2 yr. and in 13 more than 2 yr. before tumor onset. It was also felt that hormonal factors may secondarily influence the growth of desmoid tumors. Among 6 case histories reported in detail is one of colonic polyposis with excessive desmoid infiltration in the abdominal scar, which may be an example of Gardner's syndrome.

64-135 OVARIAN FIBROMAS AND MESENTERIC CYSTS: THEIR ASSOCIATION WITH HEREDITARY BASAL CELL CANCER OF THE SKIN. (E.) Clendenning, W. E. (NCI, Bethesda), J. R. Herdt and J. B. Block. *Am. J. Obstet. Gynec.* 87(8):1008-1012, 1963.

This report describes 5 female pts. with a rare hereditary syndrome (called basal cell nevus syndrome) whose major features consist of mandibular cysts, basal cell cancers of the skin and minor rib anomalies. In 3/5 pts., calcified ovarian fibromas were found; concomitant mesenteric lymphatic cysts occurred in 2/5 pts. At the time of publication another woman with this syndrome was seen.

64-136 PRIMARY CARCINOMA OF THE LIVER: OBSERVATIONS IN NORTH GENERAL HOSPITAL. (E.) Tolentino, A. D., Jr. *Philipp. J. Cancer* 5(1):423-433, 1963.

In studies conducted at North General Hospital in the Philippines, primary carcinoma of the liver was revealed in 16/500 autopsies in adults (3.2%). In the U.S., hepatic cancer is seen in less than 1% of the adult autopsies. Incidence of hepatic carcinoma is higher in cirrhotic pts. than in non-cirrhotic pts. both here and abroad. In American males hepatic cancer is usually seen above age 50; in Filipinos the majority is noted between 31-50 yr. of age. Although metastatic carcinoma of the liver was found in only 7/500 adult autopsies, the author feels that incidence is probably even higher than that of primary carcinoma in the Philippine Islands.

64-137 MALIGNANT AND PRE-MALIGNANT LESIONS OF THE ORAL CAVITY. OBSERVATIONS IN NORTH GENERAL HOSPITAL. (E.) Tolentino, A. D., Jr. B. C. Erese and O. L. Soriano. *Philipp. J. Cancer* 5(1):406-416, 1963.

In a total of 455 (3.18%) oral lesions found in 14,324 surgical specimens during a 5-yr. period (1957-1961) at North General Hospital in the Philippines, 168 cases of epidermoid carcinoma were encountered (93 females, 75 males). This constituted 1.2% of all surgical specimens, 37%

of all oral lesions and 90.3% of all malignant oral lesions (mostly in 50-60-year age group). Leukoplakia appeared in 68/455 oral lesions. In the oral cavity, epidermoid carcinoma was localized as follows: palate (31.2%), buccal mucosa (25.3%), tongue (23.1%), gingiva (11.3%), lip (8.0%), floor of mouth (1.1%). The most frequent site for epidermoid carcinoma of oral cavity was the inner cheek mucosa in males (63%) and the palate in females (73%). Peculiar habits, like inverted cigarette smoking in older women and betel-nut chewing in older men, were cited as contributing factors.

- 64-138 HEREDITARY DEFICIENCIES OF CLOTTING FACTORS VII AND X ASSOCIATED WITH CAROTID-BODY TUMORS. (E.) Kroll, A. J. (Massachusetts Eye Ear Infirm., Boston), B. Alexander, F. Cochios and L. Pechet. New Eng. J. Med. 270(1):6-13, 1964.

Finding of a prolonged Quick prothrombin time (22-37%) in a 47-year-old woman led to the investigation of 242 individuals (4 generations) of her family. Carotid body tumors were detected in 12 individuals (3 males, 9 females), 5 of which were bilateral. Clotting defects were found in 8/12 subjects with carotid body tumors. Mild to moderate decreased factor X was found in 60/242 subjects, 49 of whom had levels below 50% and 8 below 20%. Mild diminished factor VII (range, 19-65%; mean, 46.5%) was found in 28/242 subjects. Transmission of both clotting defects was autosomal intermediate, and that of the carotid-body tumors autosomal dominant. The possible genetic interrelation of the 3 abnormalities is discussed.

- 64-139 LEUKAEMIA CLUSTERS. (E.) Rewell, R. E. (Women's Hosp., Liverpool, England). Lancet 2:882, 1963.

Several yr. after a woman (aged 40) died of acute leukemia in Women's Hospital, it was learned that she was brought up in a suburb of Birkenhead, and that of the dozen or so children who were her companions in that small area over that time, no less than 4 had died of acute leukemia within 3-4 yr. of each other, and all around age 40.

- 64-140 HEREDITARY FACTORS IN HUMAN LEUKAEMIA: A REPORT OF FOUR CASES OF LEUKAEMIA IN A FAMILY. (E.) Gordon, R. D. (Alfred Hosp., Melbourne, Australia). Aust. Ann. Med. 12(3): 202-207, 1963.

The author presents 4 cases of leukemia occurring in a family during two generations. These included a 47-year-old woman with acute myeloblastic leukemia, her 29-year-old nephew who had acute myeloblastic leukemia and her 58-year-old sister who had acute leukemia, type uncertain. The fourth case, a 2.5-year-old niece, unsubstantiated

by medical records, is based upon a death certificate diagnosis of acute leukemia. No cases of mongolism, sex chromosome abnormality or consanguinity in the family, nor exposure to irradiation or to any carcinogenic chemicals or drugs on the part of persons afflicted has been demonstrated. The report is at variance with the recorded high incidence of lymphatic leukemia in familial cases.

- 64-141 CARCINOMA OF THE PROSTATE IN UGANDA AFRICANS. (E.) Dodge, O. G. (Dept. Path., Sheffield U., England). Cancer 16(10): 1264-1268, 1963.

Carcinoma of the prostate accounted for 3.8% of all cancer in male pts. reported by the Kampala Cancer Registry for the yr. 1952-1959. Among 97 cases, 57 were diagnosed histologically (3 undifferentiated, 1 squamous cell, 53 adenocarcinomas); peak incidence in the histological series was at age 55-74 yr., in the clinical series, 45-75+ yr. The tumors appeared to arise at a lower av. age than in Europeans, but did not differ in histological pattern. Occult carcinomas (not included in this series) are also known to occur. The incidence (adjusted for age) of prostatic carcinoma in Kyadondo county, estimated at 2.41/100,000 population was compared to that of the USA (white and non-white) and Norway (14.105, 21.029 and 11.353, resp.).

- 64-142 AUTOPSY FINDINGS IN THE OCCUPATIONAL PATHOLOGY INSTITUTE OF GELSENKIRCHEN. A STATISTICAL COMPARISON WITH HOSPITALS OF PATHOLOGIC INSTITUTES WITH SPECIAL CONSIDERATIONS OF THE LOCALIZATION OF CANCER IN SILICOSIS. (Ger.) Knopp, J. (Inst. Path., Gelsenkirchen, Germany). Int. Arch. Gewerbepath. 20(4):316-336, 1963.

A statistical comparison of autopsy data is presented for a number of 5-year periods (7 among 3 German hospitals and 1 in a hospital of Venezuela, South America). In the Occupational Pathology Institute of Gelsenkirchen, a total of two 5-year periods was evaluated with consideration of presence or absence of silicosis, its degree, and concurrence of other diseases. In comparison to a certain 5-year period (in the hospital Berlin-Moabit) taken as a Standard (100%), the relative incidence of cancer in silicosis pts. among the Institute autopsies was approx. 100% in light and moderate silicosis cases, and only 70% in severe silicosis cases. Localization of cancer was analyzed and it was concluded that the absolute number of cases of bronchial carcinoma tended to increase in the cases of light or moderate silicosis and to decrease (or to be masked) in severe silicosis cases.

- 64-143 THE IOWA BLOOD TYPE DISEASE RESEARCH PROJECT: II. (E.) Buckwalter, J. A. (Dept. Surg., State U. Iowa Coll. Med., Iowa City), C. B. Pollock, G. Haselton, J. A. Krohn,

J. Nance, J. L. Ferguson, R. L. Bondi, J. J. Jacobsen and A. H. Lubin. J. Iowa Med. Soc. 59(2):58-66, 1964.

Data accumulated between 1958-62 by the Iowa blood type disease research project showed no association between gastric carcinoma and ABO blood groups which is characterized by world studies showing increased incidence in persons with type A blood. An association between carcinoma of the lung and ABO groups was not established. Association between intracranial neoplasms and blood group A was of borderline statistical significance. The findings of a decrease in the incidence of esophageal carcinoma and pancreatic carcinoma in pts. with blood group O and the increased incidence in the other 3 types, especially type B, were not statistically significant but when they were combined with those reported by other investigators and analyzed by the Woolf method, results were significant. The findings in carcinoma of the cervix and of the body of the uterus were statistically significant when compared with the controls or each other but when the cervix and uterine body findings were combined and compared with the controls, no evidence of an ABO blood group effect was seen. The decreased incidence of ovarian carcinoma (445 pts.) with type O and increased incidence in type A was not statistically significant. In gastric carcinoma pts., statistically significant increases were found in the frequencies of R₁R₂ genotypes, while there was a significant reduction in the frequency of R₁ and R₂ genotypes. These findings may represent an effect resulting from the transfusion of rhesus-positive and MN-incompatible RBC.

64-144 THE INCIDENCE OF CANCER OF THE UTERUS IN THE PEOPLE'S REPUBLIC OF CROATIA.

(E.) Dekaris, M. (Dept. Gynec. Obstet., U. Zagreb, Yugoslavia), B. Krznar and Z. Kulcar. J. (Liječn. Vjesn.) 84(8):1-7, 1962.

Minimal substantial changes in uterine cancer incidence and treatment have been noted at the Gynecology Clinic of Zagreb in the period following the first postwar Congress of Yugoslav Gynecologists, held in 1950. Early systematic detection has accounted for higher carcinoma of the cervix incidence today (17.0%) as compared to 1950 (12.0%). Slovenia, especially, shows treatment of many more pts. with carcinoma of the cervix between the ages of 29-39 yr. than does Croatia. In the last 3 yr., the mortality rate for carcinoma of the cervix was about 5 in 100,000 with the highest rate in the 70+ yr. age group. Records of 6592 pts. under medical care from 1944-1960 show that the largest number of cases of carcinoma of the cervix were found in the 49 yr. age group in Croatia and the 50-59 yr. age group in Slovenia.

64-145 CHROMOSOME ANOMALIES IN WALDENSTROM'S MACROGLOBULINAEMIA. (E.) Heni, F.

(Clin. Med., U. Tubingen, Germany) and H. Siebner. German Med. Monthly 9(2):72-73, 1964.

In a 37-year-old woman with Waldenstrom's macroglobulinemia who obtained subjective improvement from small doses of prednisone, sternal bone marrow cultures showed an extra chromosome in 18.4% of the mitoses with a centrally placed centromere and in size it fell between chromosomes number 2 and 3. This chromosome differs in size and shape from those previously described in this disease and tritiated thymidine studies suggested that it was derived from 1 of the autosomes of Group A. The chromosome anomaly was thought to be the cause of the disease.

64-146 CHILDHOOD MALIGNANCIES - A STATISTICAL SURVEY. (E.) Ramakumar, L. (Dept. Pediat., Government Coll. Med., Patiala, India), S. C. Sood and S. P. Diwan. Indian J. Child Health 12(3):190-195, 1963.

Records of 12,760 children (age 0-12 yr.) admitted to Rajendra Hospital, Patiala, India, from 1958-1961 showed 117 cases (0.92%) of malignancy in the following order of frequency: 29 pts. with leukemia (21 acute, 6 chronic myeloid, 2 chronic lymphatic; 24.7% of total malignancy); retinal gliomas (17); Wilms's tumor (15); intracranial tumors (14); Hodgkin's disease (9); lymphosarcomas (7); neuroblastomas (6); retinoblastomas (5); teratoma (3); nasopharyngeal carcinoma (3); fibrosarcoma of the hip (2); and 1 case each of abdominal melanoma, carcinoma of the stomach, carcinoma of the colon, chondroma, Ewing's sarcoma, undifferentiated mediastinal lymph node tumor, and mixed parotid tumor. Statistically significant is the fact that malignancies are 3.5-4x more common in males at all ages and for practically all types of malignancies. The age range with the greatest incidence of cancer in this study was 3-6 yr.

64-147 CHROMOSOME ABNORMALITIES IN MULTIPLE MYELOMA. (E.) Bottura, C. (Dept.

Clin. Med., Ribeirao Preto Sch. Med., Sao Paulo, Brazil). Acta Haemat. (Basel) 30(5):274-279, 1963.

No chromosome abnormalities were detected in the bone-marrow cells of 3/5 untreated pts. with multiple myeloma. In a 42-year-old man, only one out of 35 metaphases analyzed showed an abnormal karyotype. A 61-year-old man showed 45 chromosomes in the majority of cells and the missing one was a small acrocentric autosome (either 21 or 22). The Y chromosome appeared to be present, and an XY/XO mosaicism prior to disease was considered unlikely.

64-148 GENERAL CHARACTERISTICS OF MORTALITY DURING 1947-1960 IN THE PEOPLE'S REPUBLIC OF BULGARIA. (Bul.) Paskalev, T. Surv. Med. (Sofia) 14(10):3-18, 1963.

While the mortality rate, due to various diseases, between 1947-1960, as a rule decreased, the rate increased in cases of neoplasms and circulatory diseases. While in 1947, 86 (per 100,000) died from the cancer, in 1960, the rate was 113. The increase was in all age groups but particularly so in group age over 40 yr. The death rate due to neoplasm in the groups age 0-1, 1-4, 5-9, 10-14 and 15-19, in 1947, was 0.4-1.0 per 10,000, and in 1960 it was 0.3-1.1, thus indicating no increase in death rate. In the age groups 20-59 yr. of age it was 0.5-23.6 per 10,000, in 1947, and 0.6-24.7 in 1960. The highest figures, 50.1 and 77.5/10,000, resp., were obtained in the 60 or over groups.

64-149 MORBIDITY STATISTICS FOR THE LEUKEMIAS. AN ANALYSIS OF 3493 CASES OF LEUKEMIA IN THE TUMOR STATISTICS OF THE GERMAN DEMOCRATIC REPUBLIC FOR THE PERIOD 1953-1957. (Ger.) Stobbe, H. (1st Clin. Med., Charite Clin., Berlin), G. P. Wildner and W. Schuckmann. *Deutsch. Gesundh.* 18(47):2029-2034, 1963.

Among East German pts. with leukemias, the percentage distribution of incidence of chronic lymphatic (CLL), acute (AL) and chronic myeloid leukemia (CML) remained essentially constant during the 5-yr. period 1953-1957: 40.4, 31.3, and 28.3, resp. Among male leukemic pts. only, comparable tabulations were 47, 28, and 25, resp.; among female pts., 33, 35 and 32. Of all new cases of CLL, AL, and CML, resp., 69.14%, 53.44%, and 55.36% occurred in males. The approx. total incidence/100,000 population of CLL was 1.3, 1.3, 1.6, 1.8, and 2.0 in 1953, 1954, 1955, 1956, and 1957, resp.; that of AL, 1.0, 1.0, 1.1, 1.3, and 1.6, resp.; that of CML, 1.0, 1.0, 1.1, 1.0, and 1.25, resp. In males, the incidence of CLL increased sharply and progressively in the age groups from 50-75, and then declined abruptly; an identical trend in females involved much less overall increase, with approx. 85% in pts. over 50. In both men and women, the incidence of AL was essentially constant up to age 55; then showed a slight increase (which was somewhat greater in males) between 55-80. In both men and women, the incidence of CML increased progressively from age 20-70. In males the rate was slightly greater from age 25-40 and again from age 55-60; at a slightly greater rate for females from age 40-50 and again between age 55-68. In males, the rate of incidence remained essentially constant from age 75 on; in females,

it dropped abruptly, to approach the same rate as that seen at age 5-25. The percentage incidence of leukemias in relation to other neoplasms is also presented graphically, by age group, separately for men and women. In both boys and girls, childhood leukemias showed a markedly greater rate of incidence prior to the 9th yr. of life (with a secondary, slight increase in boys at age 10 and girls at age 13). Maximal incidence, in both sexes, was from age 4-5.

64-150 CLINICAL CHARACTERISTICS OF LIVER PRIMARY CANCERS (55 PERSONAL CASES).

(Fr., Abstract) Bonfils, S., L. Demeulenaere, P. Bernades and M. Laurijssens. *Lyon Med.* 210(48):1146-1147, 1963.

In a brief description of 55 pts. (30 French and 25 Belgian) with primary cancer of the liver, the authors report that 60% were over age 60 at the time of appearance of the condition and that the majority (67%) were men. Alcoholic cirrhosis was present in the history of 25% of the cases. Hemochromatosis and hepatitis were also suggested as possible, although rare, etiologic factors.

64-151 CANCER MORTALITY IN THE CITY OF MEDELLIN. (Sp.) Robledo Clavijo, A. (Dept.

Epidemiol., Dept. Public Health, Medellin, Colombia). *Antioquia Med.* 13(10):745-747, 1963.

In the city of Medellin during the years 1960, 1961 and 1962 cancer mortality ranked third in importance after infectious and parasitic and cardiovascular diseases, with 110-113 deaths per 100,000 people. Most frequent sites were (in decreasing order) stomach, trachea, bronchi, lungs, mammary gland, oropharynx and esophagus.

64-152 SEASONAL CHANGES IN ITALY FROM 1955 TO 1961 IN THE MORTALITY FROM VARIOUS DISEASES (PULMONARY TUBERCULOSIS, EXTRAPULMONARY TUBERCULOSIS, TUBERCULOSIS IN GENERAL AND TUMORS). (It.) Fronzaroli, L. (Dept. Sanit. Statist., U. Rome). *Lotta Tuberc.* 33(10):662-678, 1963.

A study of official records of all of Italy revealed a progressive increase of cancer deaths from 1955 to 1961 (26%), with highest peaks recorded for 1955 and 1956. Patients with this condition died most frequently in October and November, 739,008 and 700,101, resp.

See also abstract nos.: 6,16,17,50

MISCELLANEOUS

- 153 MALIGNANT TUMORS OF THE LIVER. EXPERIMENTAL HEPATOMA IN THE RAT. (Fr.) Breton, E., J. Boy, E. Chany, C. Frayssinet, Jacob, Y. Moulé and A.-M. de Recondo. Lyon 210(48):1143-1144, 1963.

the absence of any evidence of specific morphologic or biochemical differences between the cells of malignant hepatomas and normal hepatocytes, the factors responsible for the acquisition by a cell of new genetic characteristics would appear to consist of thus-far undetectable disturbances underlying modification of nucleic acid and protein macromolecules. In the presence of such modification, in turn, both the incidence and latency periods of hepatomas induced by carcinogens which are not hepatotoxic would appear to be a function of particular patients' ages, sex, and hormonal and nutritional states--factors which may also be responsible for determining a particular tumor's morphologic characteristics. (Although the same sequence and factors might be operative in the case of hepatomas induced by other carcinogens, both would tend to be masked by the latter's hepatotoxicity.)

- 154 CYTOCHEMICAL DIFFERENCES BETWEEN MAMMALIAN CELL LINES OF NORMAL AND NEOPLASTIC ORIGINS. CORRELATION WITH HETEROTRANSPLANTABILITY IN SYRIAN HAMSTERS. (E.) Persson, T. (Inst. Med. Cell Res. Genet., Karolinska Inst., Stockholm, Sweden), G. E. Olsson, D. Killander and G. Lomakka. Exp. Cell Res. 32(3):553-565, 1963.

cytochemical characteristics of uncloned cells derived from normal and neoplastic sources were determined by means of recently developed physical "population study technics". Dry weights of individual cells was determined by use of scanning high-resolution ultramicrointerferometry; approx. cell nucleotides were determined by measurement of "total extinction" at 265 mμ employing a rapid scanning ultramicrospectrophotometer. Cell lines derived from neoplastic sources exhibited greater variability than those derived from non-neoplastic sources with respect to the amount of cytoplasmic RNA and cytoplasmic protein (C-RNA-PR) per cell; this observation is in accord with results of earlier studies on populations of neoplastic cells derived from *in vivo* sources. Among 8 neoplastic cell lines studied, 6 (including KB and HeLa) showed a correlation between heterotransplantability at 1.0×10^4 cells in the unconditioned skin pouches of Syrian hamsters and C-RNA-PR; 3 lines were not heterotransplantable and C-RNA-PR was atypical, but resembling normal cell populations. Three normal (adult) lines were not transplantable and showed C-RNA-PR characteristic of normal cell populations. The variability of cytoplasmic protein per cell amounts of C-RNA-PR in the populations of neoplastic cells is of such magnitude

that it must represent quantitative variations in ribosomal RNA content of such cells. In view of the evidence for the participation of the nucleolar system in the synthesis of ribosomal RNA, this cytochemical variability may reflect disturbance in the nucleolus-nucleolus-associated chromatin biosynthetic system.

- 64-155 THE RELATIONS BETWEEN DNA, RNA, AND PROTEIN IN NORMAL EMBRYONIC CELL NUCLEI AND SPONTANEOUS TUMOUR CELL NUCLEI. (E.) Seed, J. (Dept. Radiother., U. Cambridge, England). J. Cell Biol. 20(1):17-23, 1964.

Interferometric and photometric measurements were made successively on individual cell nuclei from a normal mouse embryo limb bud, and tumor cells from the growing edge of a spontaneous tumor arising in the flank of a C+ strain mouse. In the nuclei of normal embryonic cells, the syntheses of DNA, nuclear RNA, and protein appear to be closely associated, whereas in tumor cell nuclei an appreciable fraction of chromatin RNA and protein synthesis is dissociated from the replication of DNA. These results are consistent with differences in cell metabolism previously reported to exist *in vitro*.

- 64-156 A REPORT CONCERNING RETINAL GLIOMA. (Ger.) Holland, G. (Eye Clin., U. Kiel, Germany) and H. Thiers. Ophthalmologica (Basel) 146(6):377-394, 1963.

In a review (41 references) concerned primarily with familial glioma retinae, the author reports that although only 3/43 of his own cases (21 men, 22 women) had a family history of the disorder, it occurred in the offspring of 2 of the 4/40 remaining pts. who had children. One pt. with bilateral glioma retinae had a child who also developed the disorder bilaterally. Another pt., with unilateral glioma retinae, had 2 children who developed the disease: 1 bilaterally (with subsequent death from cerebral metastasis) and 1 unilaterally. The 2 remaining pts. with offspring had 1 and 6 healthy children, resp. On the basis of this experience and other reports, the authors conclude that spontaneously arising, retinal gliomas may presage a familial disorder in succeeding generations, and that this risk is greatly enhanced if the spontaneous condition is bilateral.

- 64-157 MORPHOLOGICAL STUDY OF CYSTIC LUNG CANCER. (Jap., Abstract) Kondo, T. (Res. Inst. Tubercul. Lepr., Tohoku U., Japan) and H. Takahashi. Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.) 52:140, 1963.

Autopsy of a 67-year-old Oriental male revealed squamous cell carcinoma (which metastasized to a lymph node) in a cystic cavity of the lung; in this

case it was believed chronic infection (not tubercular) was a factor in the production of the malignancy. In a second case (a 38-year-old Oriental female), where there was cystic emphysema and caseous cavitation of the lung, the bronchial epithelium had become anaplastic; this was considered a possible precancerous lesion.

- 64-158 THE HISTOCHEMISTRY OF THE BASAL CELL EPITHELIOMA. (E.) Sams, W. M., Jr. (Dept. Med., Duke U. Med. Ctr., Durham, N. C.), J. G. Smith, Jr. and G. R. Finlayson. *J. Invest. Derm.* 41(6):457-462, 1963.

In sun-exposed areas there was found a band of orcein-positive, elastotic material extending from the upper third of the dermis adjacent to basal cell epitheliomas, under the tumor and back to the elastotic dermis on the opposite side. This band was frequently associated with moderately to intensely positive acid mucopolysaccharide staining. Acid mucopolysaccharide staining was also found around tumor cell nests and between individual tumor cells from both exposed and unexposed areas of the body. However, elastosis was not associated with basal cell epitheliomas from unexposed areas.

- 64-159 FUNCTION OF THE THYMUS AND GROWTH OF TUMOR HOMOGRAFT. (E.) Perri, G. C. (Sloan-Kettering Inst. Cancer Res., New York), M. Faulk, E. Shapiro, J. Mellors and W. L. Money. *Nature (London)* 200:1294-1296, 1963.

Newborn Sprague-Dawley rats were thymectomized (thyx.) within 48 hr. of birth and Jensen sarcoma was implanted when the animals were different ages (no details) with sacrifice 12-14 days later. The calculated daily growth rate of the Jensen sarcoma in thyx. rats was 1.8x greater than the tumor-bearing controls and by day 14 after implantation, the tumors in the thyx. animals were 2-3x larger than in the control tumors. The control tumors showed necrosis in the central portion, while the tumors in the thyx. rats showed little or no necrosis. In control tumors at day 14, 24% of the tumors were rejected, 36% were regressing (<5 g wt.) and 40% were fully growing. In thyx. rats, 12% of the implants were rejected, 12% were regressing and 76% were fully growing (>5 g wt.). The author believes it unlikely that circulatory insufficiency could account for tumor necrotic areas in the controls, since the thyx. animals did not have any of these areas. The data indicates that the thymus in the post-natal period is important for normal development of the immune reaction, but the mechanism of its action is unclear. Results obtained from Jensen sarcoma

implantation into splenectomized and thyx. rats did not differ significantly from those obtained with thyx. alone.

- 64-160 FURTHER OBSERVATIONS ON TUMOR EXTRACTS CAUSING HEMOLYSIS IN VITRO. (E.) Reynolds, M. D. (Boston U. Med. Ctr., Mass.) and G. H. Friedell. *Proc. Soc. Exp. Biol. Med.* 114(3):798-801, 1964.

Saline and aqueous extracts were prepared of tumors induced in Golden hamsters (70-90 g wt.) by flank inoc. of the methylcholanthrene (MCP)-induced hamster sarcoma of Lutz and a spontaneous hamster melanoma (MM2). Saline extracts (Sherman method) were prepared from the viable (peripheral) and necrotic (central) portions of 13 MCP tumors. In 8 cases, the viable extract was active and the necrotic extract inactive; in 2 cases, the reverse was true and in 3 cases, neither portion showed activity. Of the aqueous extracts prepared from viable tissue of 4 MCP and 4 MM2 tumors, 5 were active and 3 inactive. The addition of fresh hamster serum to nonhemolytic extracts of viable tumor did not activate them. Two saline extracts of normal hamster tissue (pooled lungs, adrenals and kidneys) from nontumor-bearing animals and a saline extract of autolyzed normal lung tissue showed no hemolytic activity. An aqueous extract of normal hamster tissue was hemolytic and this activity was extractable with ether; boiling the active aqueous extract for 3 min. caused complete loss of activity. The evidence obtained so far suggests that the hemolytic agent is a protein or that it is bound to protein.

- 64-161 ON THE ESSENTIAL NATURE OF COLLAGEN DISEASE AND NEOPLASM. THE 2nd REPORT: CAUSATIVE MECHANISM OF NEOPLASM OBSERVED FROM THE STANDPOINT OF HEMATOPOIETIC PHASES OF THE BONE MARROW AND THE FIELDS AND TIMES OF BLOOD DEFENSE REACTION. (Jap.) Saito, A. (Tohoku U. Sch. Med., Sendai, Japan). *Tohoku Igaku Zasshi (Tohoku Med. J.)* 66(1):20-35, 1962.

From the viewpoint of hematopoietic phases in bone marrow of the fields and times of blood defense reactions, the author concludes that the abnormal defense reactions in the body consist of abnormal antibody-antigen reactions and of abnormal cell-stimulating factor reactions. Whereas collagen disease is considered the terminal phase of this abnormal antibody-antigen reaction, neoplasm is the terminal form of cell-stimulating factor reactions and results from prolonged stimulation by second-phase factors (viral, physical and/or chemical) in a host with an unbalanced autonomic nervous system or sympathicotonia. The neoplasm develops in cell-toxic reaction areas.

ERRATA

1(11):#1855, 1964. Change title to read Smoked goods and cancer of the stomach.
ibid. Lines 3 and 5. Change smoking to smoked foods.

1(3):#393, 1963. Correct second author's name to read K. F. Galkovskaia.
1(3):#461, 1963. Line 11, change ESV(H) to RSV(H).

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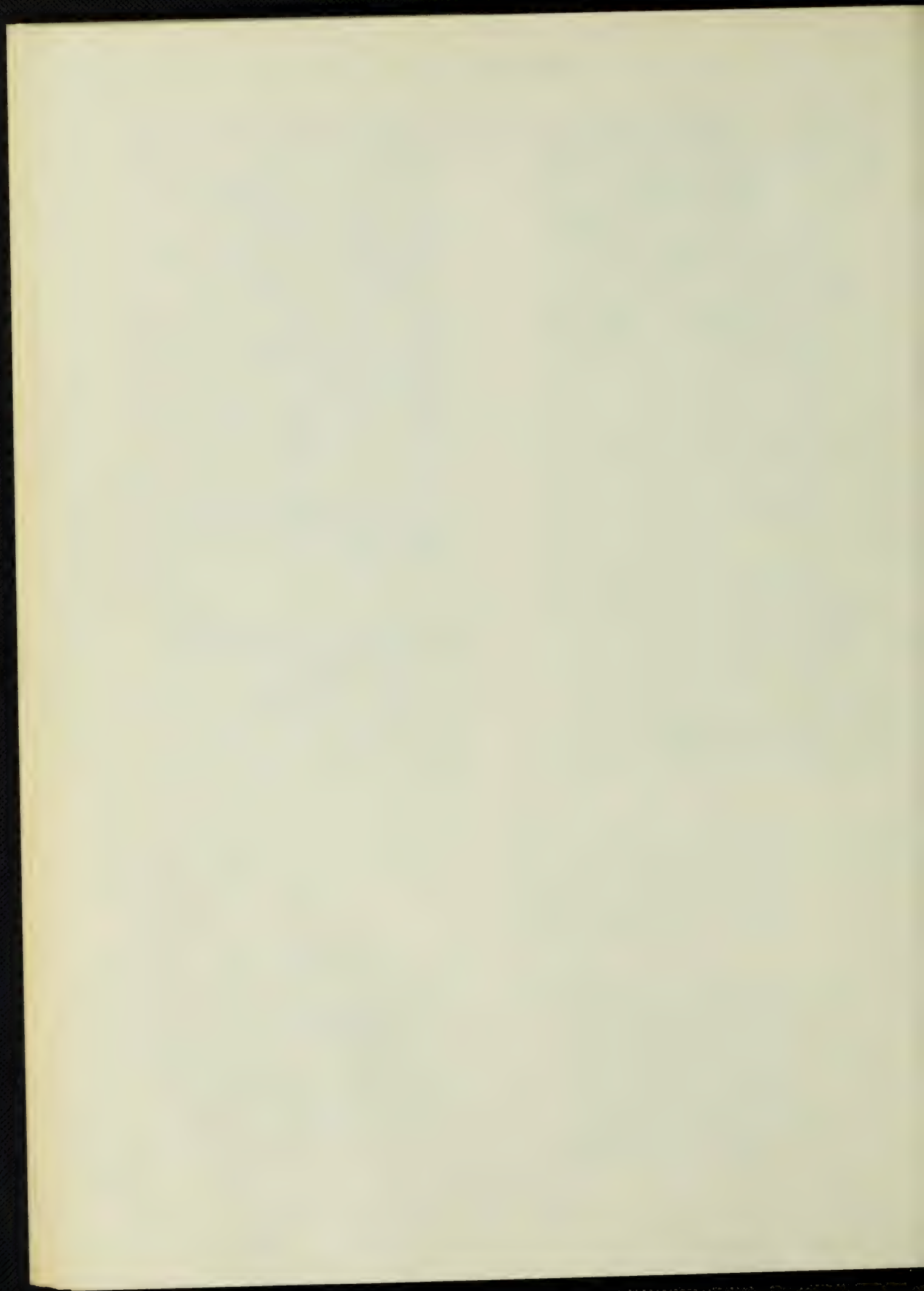
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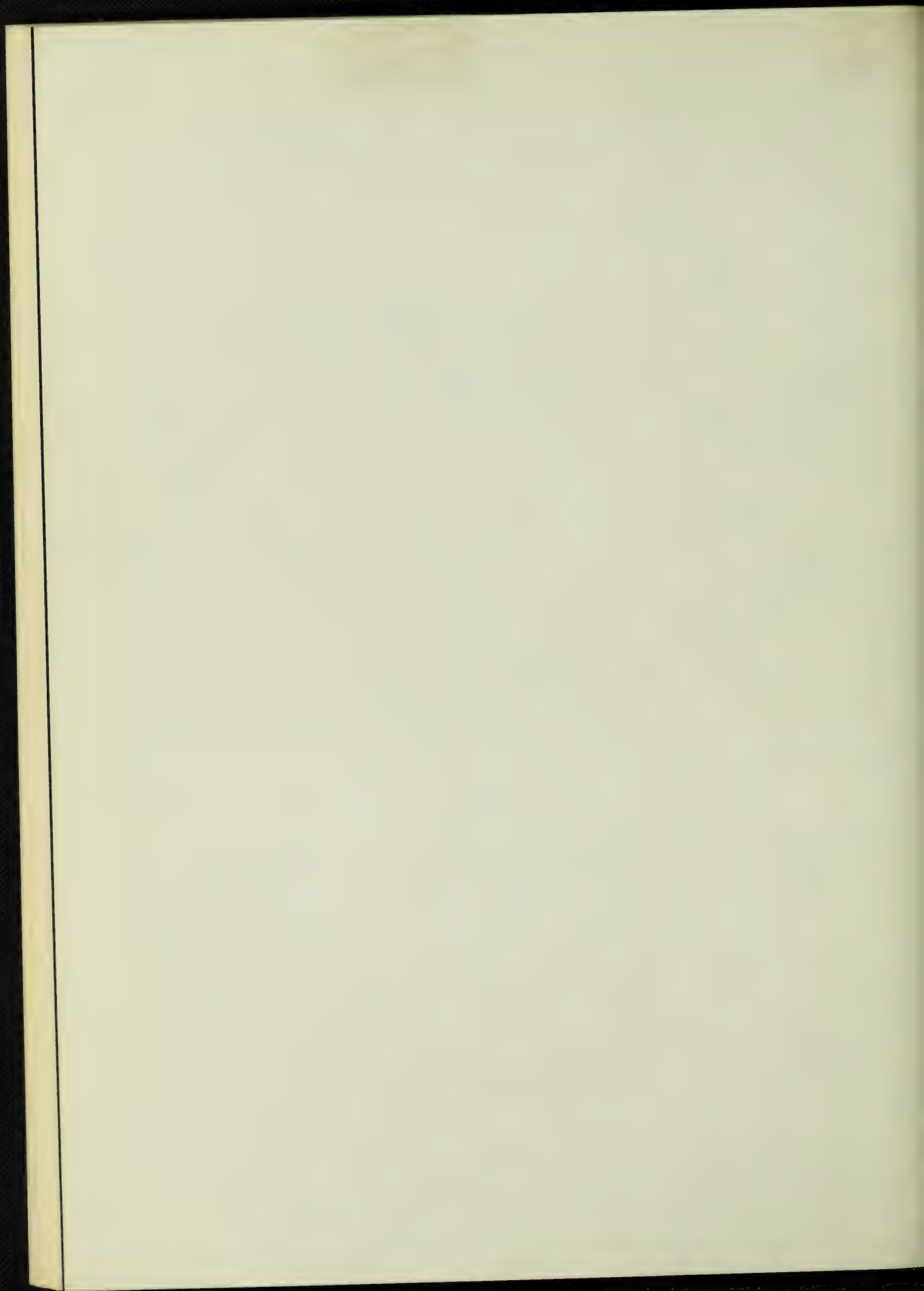
No. 2

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS ABSTRACTS

Volume 2, Number 2
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC	millicurie(s)	mm	millimeter(s)
μC	microcurie(s)	mo.	month(s)
cm	centimeter(s)	MTD	maximum tolerated dose
conc.	concentration(s)	NCI	National Cancer Institute
cpm	counts per minute	NIH	National Institutes of Health
DNA	deoxyribonucleic acid	p.o.	orally
DNase	deoxyribonuclease	PFU	plaque forming unit(s)
e.g.	for example	ppm	parts per million
FFU	focus forming unit(s)	pt(s).	patient(s)
g	gram(s)	RBC	red blood cells (erythrocytes)
μg	microgram(s)	RES	reticuloendothelial system
g.i.	gastrointestinal	resp.	respectively
Hb	hemoglobin	RNA	ribonucleic acid
hr.	hour(s)	RNase	ribonuclease
ID ₅₀	median infectious dose	s.c.	subcutaneous
i.m.	intramuscular	soln.	solution(s)
incub.	incubate(d), incubation	TCID	tissue culture infectious dose
inj.	injected, injection(s)	x	times (e.g. x 3/wk.)
inoc.	inoculated, inoculation(s)	U	unit(s)
i.p.	intraperitoneal	UV	ultraviolet
I.U.	international unit(s)	VA	Veterans Administration
i.v.	intravenous	vol.	volume
kg	kilogram(s)	WBC	white blood cells (leukocytes) or count
LD ₅₀	median lethal dose(s)	wk.	week(s)
M	molar	wt.	weight
mM, μM	milli-, or micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

162 MALIGNANT BLOOD DISEASES AND TRAUMAS.
(Fr.) Albahary, C. Ann. Med. Leg.
(Paris) 43(2):177-182, 1963.

Brief review of the literature on the association of mechanical traumas with leukemias, myelomas, Hodgkin's disease and lymphatic sarcomas. Post-traumatic malignant hemopathies are very rare. In the majority of the cases reported the effect of trauma is either insignificant or cannot be assessed; often trauma acts as a revealing factor with respect to the primary blood disease. A few observations of trauma acting as a determining factor, alone or in association with other factors, include cases of chronic myeloid leukemia diagnosed after a trauma of the left hip, a fracture of a bone, cases of myeloma sarcoma developing as single tumors at the site of bone trauma, and cases of lymphoid or myeloid leukemia arising in subjects where the primary blood disease was complicated by an infection persisting until the discovery of the primary blood disease. (10 references)

163 LIVER TUMOURS IN RAINBOW TROUT. (E.)
Editorial. Lancet 1:654, 1964.

Hepatocarcinomas or hepatocarcinomas were found to be most endemic in hatched trout all over the world (United States, Italy, France), but they do not, if ever, appear in wild trout. Whereas wild trout eat a high protein diet, hatched trout are fed pellets containing fish and meat, various cereal meals, oils, vitamin supplements and antibiotics. No virus has been demonstrated. The relationship of tumor formation to the toxic products of molds, such as Aspergillus flavus (growing on peanut meal), is under study. Also discussed is the practical application of these observations: the carcinogenic resistance in man of eating flesh from tumor-bearing animals, the future discovery of many carcinogenic products and the financial and nutritional loss involved. (See also CRA #93, 1963 and ibid., (11):#1910 and #2035, 1964) (10 references)

164 THE ENDOCRINE AND GENETIC FACTORS IN
CANCER OF THE LUNG. (E.) Editorial.
Lancet 23(1):1-15, 1964.

A brief review of data on cancer of the lung and its relationship to sex and viral factors. The experimental and clinical data on the endocrine (mainly the pituitary-adrenal system) and genetic factors related to cancer of the lung were examined. The review concludes with a brief discussion on cancer of the lung and passive smoking. (87 references)

165 PSYCHE--NERVOUS SYSTEM--NEOPLASTIC
PROCESS. NEW APPROACH TO AN OLD

PROBLEM. (Ger.) Baltrusch, H.-J. F. (Internat. Psychosomat. Cancer Stud. Group, 19 Babenend St., Oldenburg (Oldb.), Germany) and K. Austerheim. Zschr. Psychosom. Med. 9(4):229-245, 1963.

A brief review of the role of psychic factors in the development of cancers from the literature of ancient times to the 19th century, followed by a discussion of 20th century literature on this subject, including work on the incidence of given types of cancer, e.g., carcinoma of the stomach, lung, etc. in relation to ethnic or age groups, economic or social class, etc. (See also CRA 2(2):#376, 1964.)

64-166 INFLUENCE OF THE CENTRAL NERVOUS
SYSTEM ON CANCER GROWTH PROCESSES.
(Ger.) Geiger, H. (9 Lagerhaus St., Aachen, Germany). Krebsarzt 18(11/12):444-447, 1963.

A review of Japanese and German reports is presented indicating that experimental damage of the pallidostriatum in albino rats or severance of the ischiatic nerve, 5-7 days before inoc. of Yoshida sarcoma, resulted in more rapid growth and increased invasiveness of the inoc. tumor. The effect was ascribed to damage of the mesenchyme. (4 references)

64-167 CARCINOGENIC VIRUS FROM MONKEY CAUSING
TUMOR DEVELOPMENT IN MAN. (Rus.)
Parnes, V. A. (Inst. Virol., Acad. Med. Sci. USSR, Moscow). Vop. Virus. 8(6):643-649, 1963.

In a review of the literature on Yaba virus, the author cites the history of its isolation, its morphology and morphology in relation to infection, reproduction in tissue culture, experimental infection in the monkey and immunity to it, species specificity of the virus, epidemiology of infection, and infection in man. Cell-free filtrates from monkey tumors were admin. to 6 volunteers with incurable cancer. After 5-7 days the nodes appeared and grew to 2 cm in diameter, after which time they underwent resolution. As compared with monkeys, the proliferative processes and resolution of the tumors proceeded at a more rapid rate. (See also 1(3):#484, 1963 and ibid., 1(11):#1974, 1964.) (42 references)

64-168 MAMMALIAN TUMORS INDUCED BY AN AGENT
IN ROUS CHICKEN SARCOMA. (Sp.)
Ahlstrom, C. G. Acta Oncol. (Madrid) 2(1):
3-15, 1963.

A short review of the mammalian tumor-inducing properties of Rous chicken sarcoma virus, including results previously reported in CRA 1(5):#966, and ibid., (8):#1574, 1963. (24 references)

- 64-169 ETIOLOGIC FACTORS IN THE LEUKEMIAS. (Ger.) Georgii, A. (Inst. Path., U. Munich, Germany). Munchen. Med. Wschr. 106(8): 325-329, 1964.

A general review of the etiology of leukemias includes discussions of ionizing radiation, chemical carcinogens, viruses, and chromosomal abnormalities. (6 references)

- 64-170 METABOLIC FATE OF FOREIGN COMPOUNDS AND TOXICITY. (E.) Williams, R. T. (St. Mary's Hosp. Sch. Med., U. London). Arch. Environ. Health (Chicago) 7(5):612-620, 1963.

In a discussion of the metabolic fate and toxicity of foreign compounds, 2-naphthylamine was noted as being hydroxylated by liver microsomes to 2-amino-1-naphthol in man and the dog, but the cancer resulting from 2-naphthylamine occurs in the bladder; the carcinogenesis was species specific and did not occur in the rabbit. It was suggested that 2-amino-1-naphthyl glucuronide (found in the liver and transported to the bladder) or bis(2-amino-1-naphthyl)phosphate could be hydrolyzed by β -glucuronidase in the urine to 2-amino-1-naphthol and this could be the actual carcinogen. In the rabbit, 2-naphthylamine is metabolized to the non-carcinogenic phenol, 2-amino-6-phenol. The metabolic route is different for each species: in the dog, 2-naphthylamine is not acetylated and the compound is metabolized mainly to 2-amino-1-naphthol, while in the rabbit, it is acetylated to 2-acetamidonaphthalene and 2-acetamido-6-hydroxynaphthalene. With dimethylnitrosamine (D), the site of metabolism and of toxic action is the liver and to a lesser extent the kidney. This may be due to the active methylating agent of diazomethane formed from D; the toxic effect is apparent only in those tissues which metabolize the compound. Carcinogenesis by D is probably the result of methylation of nucleic acids in these tissues by the active metabolite. (22 references)

- 64-171 POLLUTED URBAN AIR AND RELATED ENVIRONMENTAL FACTORS IN THE PATHOGENESIS OF PULMONARY CANCER. (E.) Kotin, P. (Nave Bldg., NIH, Bethesda) and H. L. Falk. Dis. Chest 45(3): 236-246, 1964.

A review is presented of the importance of carcinogenic agents in the atmosphere as an etiological factor in lung cancer production. The most ubiquitous of the carcinogenic agents in the atmosphere are from the polycyclic aromatic hydrocarbons (PAH). The amount of 3,4-benzpyrene (BP; $\mu\text{g}/100 \text{ meter}^3$) in the air of various cities varied between 0.018 (Moscow) to 6.8 (Liverpool); wide variations have been reported between urban and nonurban areas in 8 states. Also reviewed are studies on the destruction of various PAH compounds under various conditions, attempts at evaluation of inhaled BP, reaction products of

aliphatic hydrocarbons and oxides of nitrogen, and effects of artificial smog on respiratory epithelium and lung tumors in mice. (21 references)

- 64-172 HODGKIN'S DISEASE--PROGNOSIS, TREATMENT AND ETIOLOGIC AND IMMUNOLOGIC CONSIDERATIONS (CONCLUDED). (E.) Aisenberg, A. C. (Harvard Sch. Med., Cambridge, Mass.). New England J. Med. 270(12):617-622, 1964.

In a review of the literature, the prognosis, treatment and etiologic and immunologic considerations of Hodgkin's disease are described. On the basis of the isolation of viral agents causing neoplastic processes in animals, and the demonstration of causative viruses in many animal neoplasms such as the mouse mammary carcinoma agent of Bittner, there is an increasingly strong suspicion that such an agent is involved in Hodgkin's disease. Presently, no discoveries in human disease parallel the isolation of causative viral agents from animal neoplasms. (71 references)

- 64-173 HORMONES AND CANCER. (E.) Foulds, L. (Chester Beatty Res. Inst., Royal Cancer Hosp., London). Practitioner 192(1149):370-375, 1964.

In a review and discussion of the role of hormones in the etiology of certain forms of cancer and the value of hormones as therapeutic agents, the author notes that generally hormones evoke neoplasia only in their recognized target tissues with the exceptions being the induction of leukemia in mice and kidney tumors in hamsters by estrogens. Hormones also modify the effects of chemical carcinogens on the breast and on the liver; they do not act as direct carcinogens in the way that benzpyrene acts on the skin, but they act by virtue of their physiological actions. The specific hormone-responsiveness of tumors depends upon the hormonal environment in which they have developed rather than on the inducing agent. (26 references)

- 64-174 CHROMOSOMAL ABERRATIONS AND CARCINOGENESIS. (Fr.) De Grouchy, J. (Clin. Med. Genet., Hosp. Child. Dis., Paris). Med. Infant. (Paris) 70(10):601-606, 1963.

In a review of chromosomal aberrations in the leukemias and other cancers, the author concludes that a major argument against chromosomal etiology of neoplasms is the existence of normal karyotypes in many cancerous tissues--although it is possible that aberrations may exist without being demonstrable by present techniques (e.g., a change similar to the transformation of a #21 into a Ph^1 chromosome, occurring in a #1). In general, the author favors the belief that chromosomal aberrations represent a change brought about by other etiological mechanisms and in turn are the proximate cause of cancer. (27 references)

4-175 ESTROGENIC SUBSTANCES AND CARCINOMA OF THE CORPUS UTERI. (Dut.) De Waard, F. Nederl. T. Geneesk. 108(12):592-594, 1964.

A review of the possible relationship of carcinoma of the body of the uterus (corpus carcinoma) to an increased production of estrogens, especially after menopause, the author reports that 85/344 pts. over 50 who had estrogen-producing tumors also had corpus carcinoma, compared with 7/221 similar pts. under 50, and that all 7 in the last group were non-ovulators and thus non-producers of progesterone. Such long standing non-ovulation (e.g., in the presence of a Kline-Leventhal syndrome) is reportedly seen in "virtually all" younger women with corpus carcinoma, as is a significantly heightened percentage occurrence of this type of tumor in postmenopausal women with a combination of obesity, hypertension and diabetes mellitus. In the light of current epidemiological studies, he concludes that the same socioeconomic influences which encourage development of this latter triad also encourage the incidence of corpus carcinoma, probably mediated by increased estrogen production in the absence of progesterone. Reported initial findings of a study to prove or disprove this conclusion which is being carried in Africa. (1) Among S. African whites, Bantus, and persons of mixed blood, a statistically significant relationship has now been established between increased (postmenopausal) estrogen production, diabetes and hypertension. (2) Among Bantus in primitive communities, all 3 disorders are extremely rare, and corpus carcinoma is actually unknown. In comparison, among menopausal and postmenopausal Bantu women in Johannesburg, hypertension is as common as among white women of the same ages and diabetes is much more frequent. In postmenopausal pts. estrogen production among obese, diabetic Bantus is considerably higher than among comparable whites. (3) No case of corpus carcinoma was found among Bantus admitted to Johannesburg's Magwanath Hospital between 1951-56, while 12 cases were confirmed histologically between 1957-62, although total admissions during the same periods were in a ratio of 2:3. (7 references)

176 Bibliography on Smoking and Health 1958-1963. Public Health Serv. Publ. 24. Bocker, D. (Ed.). U.S. Dept. Health, Education, Welfare, Washington, D.C. 59 pp., 1963.

Bibliography of the literature on smoking and health (1958-1963), prepared for the Surgeon General's Advisory Committee on Smoking and Health and including a section on neoplastic diseases.

77 TUMOR GRAFTS AND IMMUNOLOGICAL ENHANCEMENT. A CRITICAL REVIEW. (Fr.) Sin, G.-A. (Dept. Immun. Path., St. Antoine

Hosp., Paris). Rev. Franc. Etud. Clin. Biol. 8(9):927-942, 1963.

An extensive review is presented of the phenomenon of immunological facilitation (immunologic enhancement). In immunized (active or passive) animals, usually mice, tumor grafts grow faster, their survival is prolonged and they may even "take" permanently causing the host's death. Factors of variability in the degree of this enhancement include the amount of serum admin., the sex and the strain of both donor and recipient mice, and the site of tumor implantation. Reviewed and discussed are the experimental findings related to the XYZ effect of Casey, the role of the enhancing antigens and antibodies, and the mechanism by which the immunological enhancement occurs. (125 references)

64-178 VIRUSES AS THE CAUSE OF TUMORS. (Gr.) Moutousis, K. (Dept. Microbiol., U. Athens Sch. Med., Greece). Acta Microbiol. Hellen. 8(3-4):71-82, 1963.

A review and discussion on various aspects of the induction of tumors by viruses and adenoviruses. The 1963 annual symposium on cancer held at Houston, Texas, is also reviewed. (No references)

64-179 DEVELOPMENT OF CANCER FROM ORAL LICHEN PLANUS. (Dan.) Andreassen, J. O. (Rigshospitalet, Copenhagen, Denmark) and J. J. Pindborg. Nord. Med. 70(31):861-866, 1963.

Summarizing a review of the literature, the author reports that 46 cases of oral cancer have been reported as developing in pts. with oral lichen planus (o.l.p.) of 1-40 yr. duration. In relation to sex, 41% were women, whose av. age was 50 (range, 20-70). As to site, 49% of the cancers were located in the buccal mucosa, 39% in the tongue, 10% in the lower lip, and 2% in the floor of the mouth; as to type, 32 cancers were carcinomas. In various series, incidence of cancer in pts. with o.l.p. ranged from <1%-10%. Possibly contributing factors to the development of cancer were said to be irritation from teeth or dentures, previous syphilis, irritation from tobacco, and treatment with diathermy, X-ray, tannin, arsenic, trichloroacetic acid, chromic acid, or cautery. (64 references)

64-180 MECHANISMS INVOLVED IN CANCERIZATION BY IRRADIATION, CONSIDERED AT THE LEVEL OF THE CELL. (Fr.) Latarjet, R. (Radium Inst., Paris). Bruxelles Med. 43(48):1281-1289, 1963.

In a review of radiation-induced cancers and radiation-induced *in vitro* chemical and cellular changes, the author concludes that not one but at least a dozen different mechanisms may be involved in the induction of radiation cancers. Among these are said to be intracellular mutagenic

changes as a direct response to radiation, activation of latent carcinogenic viruses which were already present in the cell, depression of cellular and/or general organismic resistance to viral infection, and intercellular transfers of materials resulting in mutagenic changes in the host cell. (38 references)

- 64-181 INHALATION OF TOBACCO SMOKE. (E.)
Hammond, E. C. (Am. Cancer Soc., New York). Conn. Med. 27(8):473-483, 1963.

This paper reviews the clinical, epidemiological, histological and experimental data on the inhalation of tobacco smoke and notes that, like heavy inhalation of the other air contaminants, tobacco inhalation is detrimental to health and results in an increase in death rate from cancer and a number of different diseases. The author believes that bronchogenic carcinomas originate from epithelial lesions, since most of the epithelial lesions of the lung, composed entirely of atypical cells, were indistinguishable from the small invasive bronchogenic carcinomas. Previous studies by Hammond and Horn show that the death rate of cigarette smokers was higher than that of non-smokers by a ratio of 10.73:1 for lung cancer, 5.06:1 for cancer of the buccal cavity, esophagus and larynx and 2:1 for bladder cancer. The author relates that the degree of disease effects caused by smoking depends upon the number of cigarettes smoked/day, the number of yr. of cigarette smoking, and the extent to which the smoke is inhaled. (53 references)

- 64-182 ENVIRONMENTAL CANCER. (E.) Hueper, W. C. (NCI, Bethesda). Conn. Med. 27(8):465-472, 1963.

In a review and discussion, the author tabulates industry-related environmental carcinogens such as organic and inorganic chemicals and nonionizing radiation according to their route of exposure and their specific target organs. Also listed are the potential environmental human carcinogens known to cause tumors in various species of animals (such as estrogens, carbon tetrachloride, chloroform, DDT, tannic acid, thiourea and derivatives, 8-hydroxiquinoline, diethylene glycol, methylated naphthalenes, bergius coal, oils and tars, butter yellow, etc.) and indicated are the environmental sources of these cancer hazards. It was indicated that while a major fraction of all cancers may be attributable to the action of these agents, definite proof is only available for a rather small portion. (See CRA 1(11): #1856 and *ibid.*, #1865, 1964.) (10 references)

- 64-183 BIOCHEMISTRY OF MALIGNANT TUMORS. (Ger.) Kuhnau, J. Med. Welt 40: 2059, 1963.

A discussion on the subject of biochemistry of

malignant tumors includes general remarks on the carcinogenic as well as carcinostatic mechanisms of action of cytostatics. Relative to the possible mechanisms involved, the coenzyme DPN is the focal point of the cellular energy transfers and other metabolic processes. The polyfunctional nature of cytostatics and carcinogens is reflected in the inhibition of glycolysis and protein synthesis, and in the changes in RNA and DNA of the cell (e.g., loss of genetic blueprint); these effects may lead to tumor genesis as well as to tumor inhibition. (No references)

- 64-184 THE LEUKEMIA VIRUS. (Jap.) Ichikawa, Y. (Inst. Virus Res., Kyoto U., Japan). Igaku (Medicine) 20(8):555-559, 1963.

A review of literature concerning the leukemogenesis of certain types of virus discussed from the standpoint of biochemistry, immunology, genetics and electron microscopic appearance. The author was convinced of the ability of virus to produce leukemia of the mouse and chicken by such evidence as transmissibility by cell-free extracts from a leukemic animal, serial passage without loss of leukemia producing ability of the virus, specific antigen formation and specific granules on the surface of the cell when observed under the electron microscope. (51 references)

- 64-185 VIRUSES ISOLATED FROM MONKEYS WITH SPECIAL REFERENCE TO THE VACUOLATING SIMIAN VIRUS 40 (SV40). (Rum.) Fenyves, A. and S. Klein. Stud. Cercet. Inframicrobiol. 14(6): 783-799, 1963.

An extensive review of all known simian viruses (classification, growth in culture, properties and potential pathogenicity) along with all known data from the literature on the SV40 group. SV40 is the only carcinogenic simian virus found thus far. Although it is not known to be carcinogenic in man, the fact that it has such marked effects in some animals (hamsters) and various tissue cultures, should make it the object of careful investigation, especially since it can be found in many cases as a contaminant in various polio vaccines (as shown by the appearance of specific antibodies in recipients) and by the appearance of anti SV40 antibodies in the sera of persons in contact with monkeys. (81 references)

- 64-186 LEUKEMIA. (E.) Frei, E. III (NCI, Bethesda) and E. J. Freireich. Sci. Amer. 210(5):88-96, 1964.

A discussion of the types, treatment and causes of acute and chronic lymphocytic or granulocytic leukemia; although the fundamental cause of human leukemia remains unknown, possible contributory factors include ionizing radiation (when the dose is greater than 200 rads), heredity, abnormal chromosomes such as the Philadelphia chromosome,

the age of the pt. and viruses. The authors note that the theory of origin of leukemia is consistent with the genetic hypothesis that the hereditary material of the cell, the DNA, has been altered. In order to cure leukemia, it is probably necessary to eliminate the entire population of leukemic cells; J. Furth showed that leukemia can be produced in animals by the inoc. of a single leukemic cell, while H. E. Skipper indicated that the cure of transplanted rodent leukemia necessitates the destruction of all the leukemic cells. (5 references)

4-187 THE PROBLEM OF LUNG CANCER. (E.) Viswanathan, R. J. Indian Med. Assn. 2(3):134-135, 1964.

In a review and discussion, the author discusses factors which have a causal association with lung cancer throughout the world but with emphasis on India. Besides accounts of the incidence of lung cancer, and the correlation between lung cancer and air pollution, cigarette smoking and age, a discussion of the intrinsic and extrinsic factors that play a part (in different proportions) in the genesis of lung cancer is presented. (13 references)

4-188 AIR POLLUTION, LUNG CANCER, AND CHRONIC LUNG DISEASE. (E.) Eckardt, R. E. Med. Res. Div., Esso Research & Engineering Co., Linden, N.J.). J. Occup. Med. 6(4):184-188, 1964.

A review is presented of the possible relationship between air pollution and lung cancer and other chronic lung diseases. A number of studies are presented which throw doubt on the causal relationship between air pollution and health effects. Essentially the author believes that while there is a strong suggestion of causal relationships between disease and air pollution, much more research is necessary to establish them. (24 references)

4-189 THE SEARCH FOR HUMAN TUMOR VIRUSES. (It.) Dmochowski, L. L. (U. Texas, D. Anderson Hosp., Houston). Rendic. Ist. p. Sanit. 26(10-11):757-769, 1963.

A presentation in Italian of part of the material previously abstracted as CRA 1(8):#1433, 1963, which includes 32 electron micrographs. (48 references)

64-190 VIRUSES AND CANCER--A REVIEW. (E.) Cooney, J. P. (Am. Cancer Soc., 521 W. 57th St., New York). Hawaii Med. J. 23(4):267-272, 1964.

A general review of both historical and current evidence in the literature supporting the concept of the viral causation of cancer. (39 references)

64-191 PRELEUKEMIC CONDITIONS. (Fr.) Duhamel, G. (Dept. Med., U. Paris/Sorbonne). France Med. 26(10):593-601, 1963.

A general discussion on symptoms and precursors of leukemia, including moderate leukocytosis, hemolytic anemia, anemia, bone marrow aplasia, and on the role played by ionizing radiations and benzene in the induction of leukemia. (9 references)

64-192 ON THE MECHANISM OF LYMPHOID RADIATION LEUKEMOGENESIS IN THE MOUSE. (Fr.) Duplan, J. F. (Radium Inst., Paris) and R. Latarjet. Nouv. Rev. Franc. Hemat. 4(1):5-10, 1964.

In a short review discussing the role of radiation in lymphoid leukemogenesis and the related experimental evidence, the authors conclude that none of several proposed mechanisms (such as direct activation of a latent virus, or action on a provirus-cell complex with subsequent production of active virus, or lowering of the defense systems of the organism in the presence of initially low amounts of active virus) offer a satisfactory explanation of the phenomenon. Accumulated experimental evidence suggests that the role of radiation is essentially indirect and consists in the production of a disequilibrium of the mechanism controlling lymphopoiesis; the result would be a hypersecretion of lymphotropic hormones by the thymus. The same can be postulated for spontaneous leukemia in AKR mice. In these animals the presence of lymphotrope hypersecretion would be a congenital factor. The shortening of the latency period of leukemia seen in AKR mice following irradiation indicates that a hyperproduction of lymphotropic hormones might occur also in this case. In a parallel manner, the virus, finding in these cells a medium favorable to its multiplication, would increase its conc. and cell-free extracts prepared from leukemic tissues would show leukemogenic activity. (23 references)

See also abstract nos.: 224,368

PHYSICAL CARCINOGENESIS

- 64-193 **PHYSIOLOGICAL DETERMINISM IN THE FORMATION OF MELANOTIC TUMORS IN DROSOPHILA (D. MELANOGASTER). EFFECTS OF HEAT AND IRRADIATION.** (Fr.) Ghelelovitch, S. (Pasteur Inst., Paris). *Bull. Assn. Franc. Cancer* 50(3):399-411, 1963.

In the larvae of certain strains of *D. melanogaster*, an hereditary predisposition to melanotic tumefaction has been shown to depend on a dominant gene in chromosome 2, which also contains genes determining the color of the eyes and development of vestigial wings. Heat and irradiation have been found to affect the tumoral transformation of the somatic cells in these larvae. X-irradiation increased not only the tumor incidence at the population level but also the size and the number of tumors at the individual level, whereas protracted exposure to heat (30°C for 24-48 hr.) resulted in complete inhibition of the carcinogenesis in a certain number of larvae but did not affect the size or the number of tumors of many larvae. After combined heat and irradiation, even when the tumor incidence was reduced by the heat exposure to values below those observed in controls, tumors maintained the size found after irradiation. However, the heat inhibitory effect was less extensive in irradiated than non-irradiated larvae, regardless of stage of larval life (although in both irradiated and non-irradiated larvae heat sensitivity increased with the age while the reverse was true with irradiation alone). The heat effect was greater when applied during days 1-2 of larval life (tumor incidence reduced from 64.1% to 32.1%) in non-irradiated larvae, but was ineffective in larvae which had been irradiated at the age of 24 hr. Exposure of larvae to heat for increasing periods of time indicates that there is a threshold for the heat effect which appears to be increased by irradiation. On the basis of these results, it is concluded that irradiation increases the sensitivity of the larvae somatic cells to the (genetically determined) tumor-inducing factor, the probability of tumor appearance depending both on the level of this sensitivity and the magnitude of the carcinogenic stimulus. Heat exposure appears instead to interfere with a third factor, which promotes initiated tumors with an "all or nothing" type of effect.

- 64-194 **LIGHT AND ELECTRON MICROSCOPIC STUDIES ON THYROTROPIC PITUITARY ADENOMAS IN THE MOUSE.** (E.) Lundin, P. M. (1st. Dept. Path., U. Gothenburg, Sweden) and U. Schelin. *Lab. Invest.* 13(1):62-68, 1964.

Male and female 6-week-old (C57BL xA)F₁ mice subjected to radiothyroidectomy with ¹³¹I (200 µC i.p.) and surgical thyroidectomy (thyx.) survived for >12 mo. (7 with ¹³¹I, 6 with thyx.) and had enlarged pituitary glands at autopsy. Light microscopic observations showed adenomas in 5/7 mice subjected to ¹³¹I and 2/6 mice subjected to thyx.

Both types of adenomas were composed of chromophobes or amphophils containing coarse-periodic acid-Schiff (PAS)-positive granules. Electron microscopy showed that these cells corresponded to cells having a highly developed endoplasmic reticulum, a large Golgi apparatus, secretory granules measuring about 90 mµ, and intracisternal globules resembling secretory granules corresponding to the light microscopically PAS-positive granules. Electron microscopy indicated that the tumor cells were basophils with high secretory activity which in appearance correspond to the so called thyroidectomy cells.

- 64-195 **POLONIUM-210: A VOLATILE RADIOELEMENT IN CIGARETTES.** (E.) Radford, E. P., Jr. (Dept. Physiol., Harvard Sch. Public Health, Boston, Mass.) and V. R. Hunt. *Science* 143: 247-249, 1964.

The polonium-210 (Po²¹⁰) content (in pC) in the mainstream smoke and the percentage recoverable in American cigarettes (and smoke) from cigarettes puffed artificially were: Brand A, non-filter, 0.10 and 81%; Brand B, non-filter, 0.12 and 90%; Brand C, filter, 0.088 and 82%; Brand D, filter, 0.070 and 88%, resp. From an analysis of 5-year-old cigarettes, the amount of Po²¹⁰ in fresh cigarettes is in equilibrium with the Pb²¹⁰ parent. In preliminary measurements of Po²¹⁰ in the bronchial epithelium of the lungs of smokers, local doses ranged from several hundred rem to more than 1000 rem for an individual smoking two packs a day over a 25-yr. period. The urine of nonsmokers contained very little Po²¹⁰ (mean of 0.011 pC/24 hr. in 4 pts.), while 3 smokers who smoked an av. of 2 packs/day had an av. Po²¹⁰ excretion of 0.065 pC/24 hr. It was concluded that Po²¹⁰ inhaled in cigarette smoke may act as an important initiator in the production of bronchogenic carcinoma.

- 64-196 **REMOTE CARCINOGENIC EFFECTS OF CERTAIN RADIOACTIVE COMPOUNDS.** (E.) Kochetkova, T. A. (Inst. Indust. Health Occup. Dis., Acad. Med. Sci. USSR, Moscow), G. A. Avrunina and N. D. Sagaidak. *Fed. Proc.* 22(5)(Part 2):T822-T824, 1963.

Additional data was reported for CRA 1(7):#1229, 1963. Fe⁵⁹ citrate (20 µC; total 580 rads) and Fe⁵⁹O₃ (0.1 µC; total 150 rads) did not cause lung cancer in 9 and 15 rats, resp.

- 64-197 **LUNG CANCER FROM RADIOACTIVE CERIUM CHLORIDE.** (E.) Cember, H. (Kettering Lab., U. Cincinnati Coll. Med., Ohio) and K. Stemmer. *Health Phys.* 10(2):43-48, 1964.

In male CFW rats receiving intratracheal inj. of 10, 15 and 30 µC of soluble Ce¹⁴⁴, in the form of

¹⁴⁴Ci₃ soln., and observed over a long period of time, incidence of primary lung cancer was 61/31/52 and 27/37, resp. The earliest tumor was found in a rat that died 70 days after a 100 μC inj. with an absorbed dose calculated at 1,000 rad. Most pulmonary neoplasms (19) were observed in the 6-12 mo. period following inj. 30 μC. At the 15 μC level, the earliest tumor was seen at the seventh mo. with highest number of tumors (22) observed in the 6-12 mo. period. At the 10 μC level, the first tumor was seen at the 11th mo. and others were seen as late as 570 days. One case of leukemia, cryptogenic in rats, was seen in a rat that died 195 days after a 15 μC dose. Neither cancer of the bone nor primary cancer of the liver or kidneys was found in any of the rats. (See also CRA 1(8):45, and #1447, 1963 and *ibid.*, 2(1):#29, 1964.)

198 STUDIES OF HYDROCARBONS ON MINERAL DUSTS. THE ELUTION OF 3:4-BENZOPYRENE OILS FROM ASBESTOS AND COAL DUSTS BY SERUM. Harington, J. S. (Chester Beatty Res. Inst., Ham Rd., London S.W.3) and M. Smith. *Arch. Iron. Health* 8(3):453-458, 1964.

percentage of adsorption of 3,4-benzpyrene was highest (100%) on chrysotile asbestos after 48-hr. shaking at 37°C as compared to crocidolite (40% after 6 hr.), coal (47% after 6 hr.) and amosite (10% after 48 hr.). The percentage adsorbed BP removed from dusts by serum over a 24 hr. period was 11%, 9.5% and 8.3% for coal, chrysotile and crocidolite, resp. Cyclohexane was more effective in eluting BP from coal dust (55 μg/100 mg dust) and from crocidolite (0.81 μg/100 mg dust) than serum. Serum eluted more BP (402 mg) than did cyclohexane (293 mg) from crocidolite, but equivalent amounts (serum 324 μg, cyclohexane 318 mg) were eluted from coal dust. Experiments with fat-free serum as an adsorbent for BP on crocidolite were inconclusive. The carcinogenic significance of these findings in relation to asbestos malignancy are discussed.

99 II. A REVIEW OF SOME FACTORS AFFECTING THE RADIATION DAMAGE TO BONE FROM INGESTED RADIUM. (E.) Spiers, F. W. (Dept. Med. Physics, U. Leeds, England). *Brit. J. Radiol.* 37(34):85-88, 1964.

Factors affecting the radiation damage to bone from ingested radium are reviewed in relation to sites of damage, the uptake and excretion of radium and the physical dose delivered to the bone tissues under a number of conditions of exposure. The article gives consideration to the effect of calcium metabolism suggested by Eve and others and to the departures from this model which seem likely if the known natural radium intake is to be compatible with the approx. known radium intake. It is suggested that the sensitive techniques of measurement now available could profitably be used to study natural levels of

radium in human beings at natural levels of intake and excretion. The author suggests that the diffuse deposition of calcium replacing radionuclides is more important in bone carcinogenesis than any high-activity "hot spots" which might develop.

64-200 AN AUTOPSY CASE OF ANGIOENDOTHELIOMA DEVELOPED ON THE CUTANEOUS SCAR. (E.) Maruyama, Y. (Dept. Path., Shinshu U., Japan). *Med. J. Shinshu U.* 8(1-2):49-61, 1963.

Autopsy of a 44-year-old woman with a history of X-ray therapy (50,000 r) given 10 yr. previously to a poorly healed actinomyces-infected appendectomy scar, revealed an ulcer (cutaneous angioendothelioma), the base of which arose from an area of firm granulation. The tumor invaded the scar as well as the liver, adipose, bone and myxomatous-appearing muscle tissue. Also present were cells, lymphoid in appearance, arranged in small clusters and entangled by a fine reticulin network. It was thought they may represent proliferated angiopericytes which had undergone some degeneration.

64-201 AUTORADIOGRAPHIC LOCALIZATION OF STRONTIUM 85 IN OSTEOSARCOMAS. (E.) Appelgren, L. E. (Dept. Pharm., Royal Veterin. Coll., Stockholm, Sweden), A. Nilsson and S. Ullberg. *Acta Radiol.* 1(6):459-464, 1963.

Inbred CBA mice bearing strontium 90 (Sr⁹⁰)-induced osteosarcomas which had lost their original Sr⁹⁰ content were inj. with Sr⁸⁵ (80 μC i.p.) and autoradiograms were prepared 4 hr. later. While the uptake of Sr⁸⁵ was much higher in tumor than in normal bone, the distribution was highly irregular and related to varying degrees of mineralization and degenerative changes. No noticeable Sr⁸⁵ uptake was seen in a number of small islands seen in the zone of generally intact, fast-growing tumor tissue and in the tumor's peripheral narrow zone of soft cellular tissue without detectable mineralization. The zone containing well-developed mineralized trabeculae, highly active osteoblasts and mostly intact blood vessels showed the most active uptake of Sr⁸⁵ in the autoradiograms. It was concluded that Sr⁸⁵ gave better resolution than Sr⁹⁰.

64-202 INCIDENCE OF LEUKEMIA IN ATOMIC BOMB SURVIVORS. (Jap.) Tomonaga, M. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan). *Igaku (Medicine)* 20(8):561-566, 1963.

In Hiroshima (H) 30,998/98,265 and in Nagasaki (N) 8,260/95,026 people who were exposed to the atom bomb were living within 2,000 meters (mt) of the hypocenter. Incidence of leukemia between 1946-1961 was 174 and 125, resp.; of these 137 and 52 were exposed within 2,000 mt. For H and N, morbidity rates of leukemia (per 100,000 of persons

exposed to the bomb) for the period 1947-1959 relative to the distance (mt) from the hypocenter was, resp.: 0-999, 102.04 and 101.18; 1,000-1,499, 26.96 and 53.97; 1,500-1,999, 7.12 and 10.37; beyond 2,000, 1.91 and 3.36. Combined morbidity in both cities of people exposed and not exposed, for the period 1947-1959 was 3.37 and 3.03, resp.; morbidity for all Japan for 1947-1958 was 1.96. For those exposed within 2,000 mt, peak incidence occurred in 1949 and gradually declined up to 1961. Average time (yr.) between bomb exposure to onset of leukemia was 5.0, 6.5, 6 and 8 for those exposed within 1,000, 1,500, 2,000 and 3,000 mt of the hypocenter, resp. In both H and N between 1947-1959 acute leukemia (AL) and chronic myeloid leukemia (CML) were increasing among people exposed to the bomb; the ratio AL/CML in H was 1.05, 2.58 in N and 2.33 for all of Japan (1945-1957). To explain this difference the author suggests that people in H had much more exposure to radiation than in N and died before they might develop AL; there also may have been a difference in the quality of the neutrons produced. The expected age-related incidence between 1950-1958 was overshadowed by the actual high leukemia morbidity.

- 64-203 HEMATOLOGICAL FINDINGS IN HIROSHIMA AND NAGASAKI ATOMIC BOMB SURVIVORS: A 10-YEAR REVIEW. (E. and Jap.) Wald, N. (Atomic Bomb Casualty Commission, Nat. Acad. Sciences, Nat. Res. Council, Hiroshima, Japan), W. E. Truax, M. E. Sears, G. Suzuki and T. Yamamoto. Hiroshima Igaku (J. Hiroshima Med. Assn.) 16(11,12):1082-1091, 1963.

Aside from the increased incidence of leukemia, measurement of various parameters failed to disclose any significant differences in blood values of those exposed and not exposed to the bomb.

- 64-204 ANTIGENIC PROPERTIES OF EXPERIMENTAL LEUKEMIAS. II. IMMUNOLOGICAL STUDIES IN VIVO WITH C57BL/6 RADIATION-INDUCED LEUKEMIAS. (E.) Boyse, E. A. (Sloan-Kettering Inst., New York), L. J. Old and S. Luell. J. Nat. Cancer Inst. 31(4):987-995, 1963.

No resistance was demonstrable *in vivo* upon inoc. of 2 TL+ (thymus leukemia antigen) C57BL/6 radiation-induced leukemias highly sensitive to TL antisera *in vitro* (see CRA 2(2):#205, 1964). Leukemia cells recovered after their outgrowth in immunized C57BL/6 mice lost their sensitivity to TL antisera *in vitro* and their ability to absorb specific cytotoxic activity from TL antisera. A single further passage in normal untreated C57BL/6 hosts was accompanied by complete restoration of sensitivity, even after 3 consecutive passages in immunized hosts. It was noted that the temporary changes in antigenicity may reflect an adaptational alteration affecting the entire population of leukemia cells.

- 64-205 ANTIGENIC PROPERTIES OF EXPERIMENTAL LEUKEMIAS. I. SEROLOGICAL STUDIES IN VITRO WITH SPONTANEOUS AND RADIATION-INDUCED LEUKEMIAS. (E.) Old, L. J. (Sloan-Kettering Inst., New York), E. A. Boyse and E. Stockert. J. Nat. Cancer Inst. 31(4):977-986, 1963.

A variety of antisera prepared in C57BL/6 mice against several spontaneous or radiation-induced leukemias of strain A or against a radiation-induced (C57BL/6 x A)F₁ leukemia were cytotoxic *in vitro* for the cells of 14 radiation-induced C57BL/6 leukemias and a C57BL/6 leukemia induced by urethan. The antisera were not cytotoxic for any of the normal C57BL/6 tissues studied. Cytotoxic tests with antiserum absorption indicate the presence of a common antigenic component in certain C57BL/6 leukemias and in the normal thymus and leukemias of strains A and C58. (For related study, see CRA 2(2):#204, 1964.)

- 64-206 STUDIES ON SERIAL CELL-FREE TRANSMISSION OF RADIATION-INDUCED RF MOUSE LEUKEMIA. (Jap.) Irino, S. (Dept. Int. Med., Okayama U. Sch. Med., Japan) and S. Sota. Gan No Rinsho (Jap. J. Cancer Clin.) 9(10):578-584, 1963.

Additional data is reported of a paper abstracted as CRA 1(7):#1343, 1963. Among 17 RF mice (30-40 days old) exposed to a single dose of total body X-irradiation of 450 r, during a 2-year period of observation, 4 showed lymphatic thymic type of leukemia, 5 non-thymic lymphatic leukemia; none showed myeloid leukemia. Among 53 exposed to 350 r results were, resp., 20, 20 and 1, when observed for 1 yr. Among 18 exposed to 250 r, results were, resp., 5, 3 and 0 when observed for 1 yr. In 300 untreated mice the same types occurred in 1, 1 and 0 when observed for 2 yr. When ultrafiltrates obtained from the liver, spleen, lymph glands and the thymus of mice with the induced leukemia were inj. into 16-hour-old mice of the same strain, 4/16 developed leukemia after 357, 374, 616 and 663 days.

- 64-207 THE INDUCTION OF HYPERPLASIA AND MAMMARY TUMORS WITH RADIOIODOTHYROIDECTOMY. (Sp.) Cardeza, A. F., R. Nallar and E. A. Porta. Medicina (Mex.) 44(933):72, 1964.

In all rats estrus ceased 1 mo. after radioiodothyroidectomy. Two mammary tumors (82-87.5 g) were found in 2/2 rats which were sacrificed at 6 mo.; histologically, they were pericanalicular adenomas. An atypical tumor was found in the pituitary of 1/6 rats sacrificed at 11 mo. and in 1/3 sacrificed at 14 mo.; the first rat also presented a large mammary adenoma secreting milk. Other findings in both tumor and non-tumor rats included: ovarian and uterine hyperplasia, marked mucification of the vaginal epithelium, duct and acinous proliferation of the mammary tissue with milk secretion, hyperplasia of acidophilic, basophilic and chromophobe cells of the pituitary.

See also abstract nos.: 169, 180, 182, 186, 192, 220, 228, 287, 359

CHEMICAL CARCINOGENESIS

- 64-208 QUANTITY OF CHARGE TRANSFER AND CARCINOGENIC ACTIVITY OF 4-NITROQUINOLINE N-OXIDES AND OF SOME AROMATIC HYDROCARBONS. (E.) Nagata, C. (Natl. Cancer Ctr. Res. Inst., Kyoto U., Japan), A. Imamura, K. Fukui and H. Saito. *Jap. J. Cancer Res.* 54(4):401-414, 1963.

A distinct parallelism existed between the quantity of charge transfer (measured in units of β/β^2) from the adenine-thymine pair of the DNA molecule and the carcinogenic activity of 4-nitroquinoline N-oxide, 6-chloro-4-nitroquinoline N-oxide, 4-nitroquinaldine N-oxide and 2-ethyl-4-nitroquinoline; the quantity of charge transfer was large for these compounds (0.3930, 0.4204, 0.3803, 0.3787, resp.) and exceedingly small for non-carcinogenic compounds. The quantity of charge transfer for 3,4,9,10-dibenzpyrene and NA was much larger than for pyrene. From these results it was suggested that the quantity of charge transfer is more important in carcinogenicity than is the stabilization energy. The compounds, 4-hydroxyaminoquinoline N-oxide and 6-dinitroquinoline N-oxide were exceptions to this distinct parallelism: the former (a weak carcinogen) had a small quantity of charge transfer and the latter (a non-carcinogenic compound) had the largest of all the charge transfers. Attempts to explain these exceptions were offered. The alteration of the base pairing in the Watson-Crick stereo-model of DNA resulting from charge transfer between DNA and the carcinogen is deemed to be the cause of tumor formation.

- 64-209 GROWTH PATTERN OF THE MOUSE PROSTATE GLAND IN ORGAN CULTURE AND ITS RESPONSE TO SEX HORMONES, VITAMIN A, AND 3-METHYLCHOLANTHRENE. (E.) Lasnitzki, J. (Strangeways Res. Lab., Cambridge, England). *Nat. Cancer Inst. Monogr.* (12):381-403, 1963.

Plants (grown by watchglass technic) of ventral and anterior prostate gland from C3H mice (4 wk.-mo.) showed that both sex hormones and 20-methylcholanthrene (MC) affect the mouse prostate gland directly on the cellular level and that this effect resembles that seen after admin. of the compounds *in vivo*. Young glands required additional testosterone for full maintenance but older glands are quantitatively less dependent on it. In contrast, the response to estrone was more basically altered from hyperplasia and squamous metaplasia of the alveolar epithelium in the young organ, to epithelial atrophy and stimulation of the fibromuscular stroma in the older gland. Activation in the absence of vitamin A provoked the formation of irregularly distributed squamous stratifying foci, which the addition of vitamin A could prevent. The induction of precancerous changes by MC and its modification by vitamin A are not dependent upon the age of the animal. However the modification of the carcinogen

effect (MC) by hormone (estrogen) seemed determined by the age of the gland and was similar to the effect produced by the hormone alone. Included is an extensive review (26 references) of the author's work and that of others.

- 64-210 THE MECHANISM OF THE INITIATING STAGE IN THE CHEMICAL CARCINOGENESIS. (E.) Melczer, N. (Dept. Derm., Med. U. Pécs, Hungary), M. Hamar and J. Kiss. *Oncologia* 17:39-54, 1964.

The initiating stage was studied in 120 inbred P strain mice (3 mo. old) divided into 3 equal groups and treated in the posterior thoracic region with 0.5% 3,4-benzpyrene in benzene for periods of 1, 2 or 3 wk. Disappearance of proteins (as revealed by the fluorescein isothiocyanate method) from epidermal cells, from the follicle epithelium and, in part, from the connective tissue of the skin was shown to take place early in the precarcinogenesis stage. The polarization countercurrent to mild galvanic stimulation appeared to be reduced or even disappeared during the same period. All epidermal cells, not only single cells, were shown to behave like malignant cells during the initiating stage, but this neoplastic reaction appeared to be reversible in early periods. The appearance of reparation, after treatment was discontinued, contradicts the concepts of summation of carcinogenic effect and linearity between stimulating effect and latency period in tumors. Since it was found that the connective tissue was the last to show reparation, it is suggested that its protective role is generally overestimated.

- 64-211 A TUMOR-SPECIFIC ANTIGEN IN BENZPYRENE-SARCOMA OF RATS. (Ger.) Becker, P. (Res. Inst. Tissue Growth, Max-Planck Inst., Berlin-Dahlem) and E. Knake. *Zschr. Naturforsch.* (B) 18(11):928-932, 1963.

Inbred Wistar rats (65-70 generations of brother-sister inbreeding, i.e., twin-like rats used throughout the experiments) were inj. s.c. 5x at 8 day intervals with 0.3 ml of 0.5% benzpyrene in sesame oil. The resulting tumors were excised and 3 tumor-antigen preparations were made by 3 different methods. The 3 tumor antigens were then inj. by various schedules and routes into normal closely inbred rats. At various intervals, the sensitized organs (spleen and kidneys) from these immunized rats were explanted into a total of 733 Carrel flasks; 177 control explants from untreated closely inbred rats were also made. When 2 of the 3 antigen preparations were added *in vitro* to the explants, no morphologic nor growth differences were seen between the experimental and control tissue cultures. With the third antigen preparation, while no effect was seen on the spleen explants, the kidney explants from the immunized rats showed marked granulation of the epithelial cells in the zone of growth and some cells or cell

groups of the epithelial membrane disintegrated. When the antigen was admin. again with the fresh nutrient medium, the disintegration of the experimental explants continued, while the control explants showed renewed activity of growth. The destructive effect of the homologous antigen on the explants from twin-like animals immunized against this antigen can be ascribed only to the antigen contained exclusively in the tumor tissue. This antigen-antibody reaction *in vitro* is recommended as a sensitive method of detecting specific antigens.

- 64-212 METABOLISM OF 4-DIMETHYLAMINOAZOBENZENE AND RELATED COMPOUNDS. III. METABOLITES OF 4-DIMETHYLAMINOAZOBENZENE IN RAT BILE AND INFLUENCE OF DAB FEEDING ON THEIR AMOUNTS. (E.) Ishidate, M. (Fac. Pharmaceut. Sci., U. Tokyo, Japan), Z. Tamura and K. Samejima. Chem. Pharm. Bull. (Tokyo) 11(8):1014-1021, 1963.

Bile samples from male Donryu rats 5 hr. after intragastric admin. of dimethylaminoazobenzene (DAB; 15 mg in 1 ml of olive oil) were analyzed by paper chromatography, colorimetry and other methods and found to contain 7 kinds of DAB metabolites: 4-aminoazobenzene (AB), 4'-sulfate-DAB, 4'-sulfate-4-methylaminoazobenzene, 4'-sulfate-AB, 4'-glucuronide-MAB, 4'-glucuronide-DAB, and 4'-glucuronide-AB. Data on the influence of DAB feeding on the amounts of DAB metabolites in the bile showed large fluctuations. The following relation of values from control and DAB-fed (0.06% in the basal diet x 144 days with metabolite examination made after 1, 3, 6, 11, 16, 21, 26 and 31 wk. of feeding) animals may be significant: 4'-glucuronide-DAB approx. the same as 4'-sulfate-DAB, 4'-glucuronide-MAB > 4'-sulfate-MAB, 4'-glucuronide-AB < 4'-sulfate-AB. The values increased for about 11 wk. until death from cancer resulted. Comparison of control and DAB-fed groups showed a consistently higher percentage of 4'-hydroxy-DAB and lower percentage of 4'-hydroxy-AB in the feeding groups from the third to the last wk. The promotion of hydroxylation in the first and middle stages of DAB feeding is given as the most likely explanation of the results obtained.

- 64-213 INDUCTION AND TRANSPLANTATION OF CANCER OF THE LUNG IN RATS. (E.) Mori, K. (Dept. Med. Zool., Showa Sch. Med., Tokyo, Japan). Gann (Jap. J. Cancer Res.) 54(4):415-425, 1963.

When female 2-3-month-old Buffalo rats were repeatedly inj. with 4-nitroquinoline N-oxide (0.25-0.5 mg/wk. s.c. to a total of 7.25, 11 and 15 mg) in a mixture of olive oil and cholesterol (100:5), the incidence of epidermoid carcinoma and adenocarcinoma of the lung after 223 days was 7.0% (3/43) and 30.2% (13/43); metastases occurred in 2 of these animals. Sarcomas (s.c.) at the inj. site were found in 81.3-93.9% of the animals and squamous metaplasia of the bronchial epithelium occurred in 18.8% and 15.2% of the

animals treated with 15 mg and 11 mg, resp. Almost all the rats had multicentric pulmonary adenomas. No marked changes in either the inj. site or the lung were noted in the 14 controls. A transplantable strain of epidermoid carcinoma was separated successfully.

- 64-214 DEVELOPMENT OF SUBCUTANEOUS SARCOMAS IN SWISS MICE GIVEN REPEATED INJECTIONS OF BENZENE IN OLIVE OIL. (E.) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino and I. Miyoshi. Gann (Jap. J. Cancer Res.) 54(4):427-431, 1963.

Swiss mice (5 female, 5 male) 4-5 wk. of age were treated with benzene (0.1 ml of a 1% soln. in olive oil, 1/wk. x 10 s.c.) and were sacrificed 166-249 days after start of the experiment. Five mice (2 male, 3 female) developed s.c. sarcomas which adhered loosely to skin and underlying tissues. Histologically all of the tumors were shown to be spindle cell sarcomas composed of fusiform cells with vesicular nuclei; 3 were fibrosarcomas. In transplantation trials in Swiss mice of 3 of these tumors, 2 that were transplanted into young adults failed to grow while the third, transplanted into 19-day-old suckling mice, showed positive takes in 3/6 recipients. Three wk. later the positive tumor transplants were 10 mm in diameter and were microscopically identical with the original tumor. Hepatosplenomegaly was seen in all of the benzene inj. mice but there was no enlargement of the thymus or lymph nodes. No leukemia or lymphoma was observed in treated mice.

- 64-215 COMPARATIVE STUDIES ON THE BIOLOGICAL ACTIONS OF 4-NITROQUINOLINE 1-OXIDE AND ITS REDUCED COMPOUND, 4-HYDROXYAMINOQUINOLINE 1-OXIDE. (E.) Endo, H. (Cancer Res. Inst., Kyushu U., Japan) and F. Kume. Gann (Jap. J. Cancer Res.) 54(4):443-453, 1963.

The first part of this paper reports on the s.c. inj. of 4-hydroxyaminoquinoline-N-oxide·HCl (HAQO) into female Oosama rats apparently in the same manner as reported in CRA 1(9-10):#1683, 1964. Two experimental groups (each 20 rats) given s.c. inj. in various sites of the abdominal wall showed 8/15 and 16/17 s.c. tumors in 100 day survivors; none developed in controls given only the vehicle. In the first group, despite inj. in various sites, 6/8 developed tumors in the right groin, where the HAQO was first admin. In a transplantation study, 4/10 tumors were successfully transplanted into normal rats. In a trial of the treatment of 1-day-old Ehrlich ascites carcinoma in groups of 10 female dd mice with i.p. inj. of HAQO and 4-nitroquinoline (NQO), while survival was prolonged beyond 50 days (compared to 15 days in controls), 2 mice in the NQO group developed local tumors. When Chang's liver cells were incub. for 24 hr. at 37°C in a medium containing HAQO (7 x 10⁻⁵M), intranuclear inclusions formed by this treatment were phenotypically identical with those

duced by NQO. (See also CRA 1(8):#1499, 53.)

216 DYE-PROTEIN BINDING IN THE ANIMALS ADMINISTERED WITH 4-DIMETHYLAMINOAZOBENZENE AMINE-N-OXIDE AND THE TOXICOLOGY OF 4-DIMETHYLAMINOAZOBENZENE AMINE-N-OXIDE. (E.) Hayama, H. (Dept. Biophys. Biochem., U. Tokyo, Japan) and H. Orii. Gann (Jap. J. Cancer Res.) 4(4):455-464, 1963.

Young and mature male Wistar rats were given 4-dimethylaminoazobenzene amine-N-oxide (DAB-NO; 0.3% in the drinking water). Typical hepatomas occurred in 11/13 rats which survived more than 6 mo. and 2/13 had liver adenomas within 6-12 mo.; 3/13 rats with hepatomas showed metastases in many parts of the body (lung, omentum, peritoneal membrane, etc.), and ascitic fluid accumulation was found in many animals with tumors showing progressive growth. The carcinogenic effect was weak in mice; several animals out of 10 (which survived more than 6 mo.) showed adenomas and adenomatous hyperplasia in the liver, but no malignant tumors were found within 15 mo. In DAB-NO was admin. intragastrically or i.m. in rats, mice and guinea pigs, protein binding of the dye took place at the site of inj. and in the liver, but only after i.m. inj. The amount of protein bound dye increased with the dose.

217 MALIGNANT TUMORS INDUCED IN MICE FED WITH N-NITROSODIMETHYLAMINE. (E.) Hayama, S. (Cancer Inst., Jap. Found. Cancer Res., Tokyo) and K. Oota. Gann (Jap. J. Cancer Res.) 54(4):465-472, 1963.

Male and female ddN mice were fed N-nitrosodimethylamine (total dose = 14.5-23 mg in peanut oil; 50 ppm of basal diet) for 5 mo. Among 13 mice which survived over 166 days, 4 showed adenocarcinoma of the lung; 21/22 which survived 129 days or more had multiple lung adenomas. Hemorrhagic exudates occurred in the peritoneal cavity in 10/22 mice within 2 mo. and the majority of the animals had severe but non-tumorous lesions in the liver. Two animals developed malignant hemangioendotheliomas which consisted of local proliferation of bizarre-shaped endothelial cells. The spleen was normal in most of the animals but diffuse cellular reticulosis was seen in 2 mice; 1 animal developed a hemangioendothelioma of the spleen and 1 male mouse showed anaplastic carcinoma of the right kidney.

218 THE ROLE OF DIFFERENT FACTORS WHICH CAN PREVENT EXPERIMENTAL CANCER. (Fr.) Hayama, J. (Inst. Med. Histochem., Fac. Med., U. Tokyo) and P. C.-J. Roth. Arch. Anat. Path. (Paris) 11(3):A137-A140, 1963.

Virgin female rabbits implanted s.c. with estradiol benzoate pellets (dihydrofolliculin;

dose not stated) and receiving water made alkaline with NaHCO₃ to pH 8.5, fibromas and fibromyomas developed in the abdomen as shown by exploratory surgery. Animals treated with the estrogen and drinking water acidified to pH 4.5 (with acetic acid) did not develop these tumors. If these regimens were reversed, admin. alkaline water to the rabbits previously receiving acidified water and vice versa, the rabbits receiving alkaline water developed tumors after 140-150 days, whereas in the tumor-bearing rabbits the lesions disappeared or left only cysts behind, suggesting that they had been calcified under the influence of the acidified drinking water. These experiments were repeated in R.III, C57BL and C3H mice treated with estradiol benzoate (0.2 mg s.c.) and acid (pH 4.5) or alkaline (pH 8.5) drinking water. In R.III mice of both sexes, tumors developed rapidly in those animals receiving alkaline drinking water and more slowly in the others, with av. survival times of 140 and 177 days, resp. In C57BL mice there was only 1 tumor (in the adrenal cortex) which presented a neoplastic cellular picture. In C3H females, most tumors were glandular epitheliomas; males often showed inflammation of the genital tract with kidney lesions and other non-malignant changes including seminal vesicle atrophy. Over 4 yr. of experimentation with the estradiol/alkaline drinking water regimen, 171/256 mice developed cancers.

64-219 ACUTE AND CHRONIC TOXICITY OF COTININ, AND ITS CARCINOGENIC ACTIVITY IN THE RAT. (Fr.) Truhaut, R. (Dept. Pharm., U. Paris, Sorbonne, France), M. de Clercq and F. Loisillier. Path. Biol. (Paris) 12(1-2):39-42, 1964.

Cotinine (a compound obtained by passing nascent hydrogen over dibromocotinine hydrobromide-perbromide), 0.5 g/l drinking water, induced malignancies in 12/60 Wistar rats (male and female; aged 2 mo. at the beginning of treatment). Intestinal lymphosarcomas or reticulum cell sarcomas of the mucosa of the g.i. tract were seen in 9/12 that died during mo. 9-11 of treatment. Of 3 animals that died during mo. 11-18, 1 had lymphatic leukemia with involvement of the liver and spleen; 1 had a carcinoma of the neck and cheek; and 1 had developed pulmonary reticulum cell sarcoma. One rat, among 45 that survived until sacrifice after 18 mo., showed a precancerous lesion consisting of a predominantly plasmacytic reticulogranuloma of the intestine.

64-220 HYPOPLASIA OF THE HEMATOPOIETIC ORGANS AS A PREMALIGNANT STAGE OF ACUTE LEUKEMIA. (Rus.) Krylov, A. A., V. P. Kuznechenkov, I. M. Suvorov and A. N. Chigirinskii. Probl. Gemat. 9(1):47-49, 1964.

In a presentation of 3 cases of acute leukemia, the authors stress the importance of etiological factors. In a 50-year-old female inhalation of benzene (as a cleaning agent) led to hypoplasia

of the bone marrow and the formation of multiple foci of extramedullary hematopoiesis in the spleen, lymph nodes and brain. Treatment of pulmonary tuberculosis with norsulfazol, sulfadiazine and streptomycin in a 40-year-old male led to hemocytoblastic metaplasia and 200,000 myelokaryocytes/mm³ in the sternum. The irradiation of a 27-year-old male resulted in leukopenia and aplasia of the bone marrow leading to acute reticulosis with spread to mucous membranes, larynx, trachea, bronchi, skin, lymph nodes and testicles.

- 64-221 CANCER OF THE BLADDER OCCURRING DURING TREATMENT WITH CHLORNAPHAZIN. (Dan.) Videbaek, A. *Ugeskr. Laeg.* 126(3):62-66, 1964.

Three cases are described in which cancers of the bladder developed during treatment with chlornaphazine. Two were solid carcinomas, occurring in pts. with polycythemia vera and Hodgkin's disease, resp., who had received total doses of 156.6 and 176.3 g over the course of 12 and 6 yr., resp., prior to occurrence of the bladder tumors. The 3rd pt., who also had Hodgkin's disease, received 149.5 g over a period of 5 yr., prior to occurrence of malignant urethral granulomatosis and 2 vaginal papillomas. After an additional 55 g over the next 2 yr., she developed a bladder tumor which showed the characteristics of a solid carcinoma at the periphery, those of an adenocarcinoma at the center. (The 1st pt., above, also received unspecified courses of P³², concurrently with chlornaphazine; the 2nd was treated with dicumarol concurrently during the 4 yr. preceding development of the bladder tumor. Both the 2nd and 3rd had previous histories of infectious hepatitis). The author concludes that prolonged admin. of chlornaphazine is accompanied by considerable danger of exerting a carcinogenic effect on the mucosa of the bladder.

- 64-222 PROTECTION OF ADRENAL CORTEX BY HYDROCARBONS AGAINST INJURY FROM 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.), T. F. Deuel and R. Fukunishi. *Biochem. Zschr.* 338:106-113, 1963.

A new quantitative, simple test is presented for evaluation of compounds which afford protection to the rat adrenal cortex from the damaging effect of 9,10-dimethyl-1,2-benzanthracene (DMBA). Consistent adrenal damage was produced in female 50-day-old Sprague-Dawley rats after i.v. inj. of a lipid emulsion of DMBA (3 mg or more). Complete prevention of adrenal damage after i.v. inj. of 5 mg of DMBA was obtained by pretreatment (2 days before) with several polynuclear aromatic hydrocarbons and aromatic amines: 20-methylcholanthrene (0.25-30 mg); 1,2-benzanthracene (25 mg); 6-aminochrysene (2.5-10 mg); 2-amino-fluorene (100 mg); fluorene (100 mg); and 2-naphthylamine (100 mg). No protection was

given by: naphthalene (200 mg); 1-naphthylamine (100 mg); 3'-methyl-4-dimethylaminoazobenzene (20 mg); acetylsalicylic acid (50 mg); and chloretone (30 mg). Complete adrenal gland protection only occurred, however, when 1,2-benzanthracene (10 mg x 1, i.v. inj.) was given 3-48 hr. before the inj. of DMBA.

- 64-223 THE LEUKEMOGENIC EFFECT OF JANUS GREEN B IN AMYTAL ASCITES SARCOMA OF MICE TREATED WITH O₂ AND NO. (E.) Braun, S. (Dept. Path., Péterfy Sándor Hosp., Budapest, Hungary) and M. Erdélyi. *Acta Morph. Acad. Sci. Hung.* (Suppl. 12):29-30, 1963.

The "O₂ and NO effect", previously obtained chemically only by acridine orange, was induced in amytal ascites tumor cells with Janus Green B (JGB). At the same molar conc., JGB exerts different effects, depending upon whether applied during N₂, O₂ or NO gas phases. In the N₂ phase, after ascites cell incub. for approx. 120 min., lethal ascites cell tumors were induced and the mice died within 18 days of inoc. During the O₂ gas phase, there were long latency periods (indicative of subcellular transfer) between the transformation of ascites into solid tumor (10-80%) and before the outbreak of lymphatic leukemia (the latter causing the death of 25-60% of the animals after an av. incub. period of 412 days). Similar changes were observed in the NO phase, but, so far, conversion to solid tumor (10-45%) only has been observed (lymphatic leukemia occurring in only 1% of the incub. animals).

- 64-224 CRITICAL EVALUATION OF THE CANCEROGENIC TEST WITH Δ^4 -CHOLESTENE-3,6-DIONE. (Ger.) Bruns, G. (German Acad. Sci., Berlin), K. Schubert, W. Zschiesche and G. Rose. *Arch. Geschwulstforsch.* 22(1-2):52-71, 1963.

Carcinogenic effects of cholesterol derivatives reported in the recent literature are tabulated in detail. The carcinogenic effects of Δ^4 -cholestene-3,6-dione demonstrated by F. Bischoff have not been so far duplicated. Comparative series of tests on a total of 141 male and female 8-16-week-old AB/Jena and C57BL mice failed to show a significant increase in tumor rate after 3 s.c. inj. of the agent (total dose 20 mg). The local tumors were predominantly mammary carcinomas. The questionable carcinogenic effect is dependent on the site of inj.; the tumor incidence at other sites was insignificant.

- 64-225 THE MORPHOLOGY OF MAMMARY TUMORS INDUCED BY METHYLCHOLANTHRENE IN AGENT-FREE BALB/c MICE. (It.) Olivi, M. (Cancer Res. Inst., U. Perugia, Italy), F. Squartini and G. Rossi. *Lavori Ist. Anat. Univ. Perugia* 23(3):167-201, 1963.

A total of 230 mammary tumors developed in 123/273

mary tumor agent-free virgin or breeder female B/c mice which at the age of 2 mo. had received cutaneous paintings of methylcholanthrene; 0.125-0.5% in oil; 16 drops every 2 wk. for applications). The frequency of cancer and age of its appearance were directly related to dose of MC admin.; mating and reproduction appeared to favor carcinogenesis. The incidence (%) of tumor and the av. time (in days) of tumor appearance in 3 groups of virgin mice treated with MC at conc. of 0.125, 0.250 and 0.5%, p., were: 18 and 489; 18 and 459; 44 and 324. Comparable values for breeders were: 53 and 372; 77 and 231. Histologically, the tumors were solid carcinomas (27), carcinosarcomas (11), ductal adenocarcinomas (189) and mucinous adenocarcinomas (3). Squamous metaplasia and diffuse keratinization was observed in 130 tumors. Keratinization was present more frequently in tumors of breeders (72/169) than in virgin mice (10/61). In breeders the frequency of tumor keratinization increased with dose of MC. Pregnancy and lactation also appeared to promote tumor keratinization. In a comparative discussion, it is pointed out that the MC-induced mammary tumors differed greatly in their morphology and histogenesis from those induced in the same strain by the mammary tumor agent.

- 26 BEHAVIOR OF MAST CELLS IN THE MAMMARY GLANDS OF BALB/c/Cb/Sc FEMALE MICE TREATED ORALLY WITH FOUR CHEMICAL CARCINOGENS. Caschera, F. (Cancer Res. Inst., U. Perugia, Italy), I. Paoletti and E. Bucciarelli. Lavori Anat. Univ. Perugia 23(3):203-207, 1963.

carcinogens (in almond oil, p.o., 1 mg/wk. admin. to pseudopregnant female BALB/c/Cb/Sc (6 wk. of age) only 1,2,5,6-dibenzanthracene (15 mg) induced a significant increase in number of mast cells of the mammary glands whereas after 20-methylcholanthrene (12 mg), benzo(a)pyrene (15 mg) or 9,10-dimethyl-1,2-benzanthracene (10 mg) the increase was very slight. No significant numerical changes were observed in relation to precancerous and cancerous lesions, thus indicating that mast cells exert a specific activity against the neoplastic process.

- 27 LUNG CARCINOGENESIS BY ISONICOTINIC ACID HYDRAZIDE AND ITS METABOLITES IN BALB/c/Se MICE. (It.) Biancifiori, C. (Cancer Res. Inst., U. Perugia, Italy), E. Bucciarelli, G. Santilli and R. Ribacchi. Lavori Ist. Anat. Univ. Perugia 23(3):209-220, 1963.

Following the intragastric admin. of isonicotinic acid hydrazide (INH; 2 mg/day), hydrazine sulfate (1.13 mg/day), or the sodium salt of isonicotinic acid (INS; 1.3 mg/day), resp., for 36 weeks beginning at 8 wk. of age, the incidence of tumors in male and female CBA/Cb/Se mice

was (%): 61.11 and 76.47; 76.19 and 90.47; 5.0 and 5.88 (controls 3.3 and 10.34). The majority of the mice treated with INH or HS showed multiple tumors (2-6/mouse). Of 61 tumors found in 24 of the mice treated with INH, 46 were adenomas, 8 anaplastic adenomas and 7 carcinomas; the av. age of the mice with the 3 types of tumors was 62, 83, and 65 wk., resp. Of 176 tumors found in 42 of the mice treated with HS, 138 were adenomas, 25 anaplastic adenomas and 13 carcinomas (3/13 with metastases to the paratracheal lymph nodes, all in females); the av. age of the mice with the 3 types of tumors was 62, 65, and 60 wk., resp. Controls and mice treated with INS developed single adenomas. Initial adenomatous transformation was seen, in order of frequency, as follows: in treated tumor-bearing mice, treated non-tumor-bearing mice and in control mice after the 80th wk. of age.

- 64-228 THE ELECTRON-MICROSCOPIC STRUCTURE OF A NEW TRANSPLANTABLE MOUSE ASCITES SARCOMA, INDUCED BY ISONICOTINIC-ACID-HYDRAZIDE. (E., Abstract) Kendrey, G. (1st Dept. Path. Anat., Medical U., Budapest, Hungary) and L. Cossel. Acta Morph. Acad. Sci. Hung. (Suppl. 12):27, 1963.

The mouse ascites sarcoma induced by prolonged i.p. admin. of isonicotinic acid hydrazide was studied 7-8 days after the inoc. of the animals with the ascites tumor. The anaplastic and immature cells of the tumor had few mitochondria (mostly abnormal) or none at all. The endoplasmic reticulum was poorly developed or absent and the cytoplasm had only a few free Palade granules. Extension of the Golgi apparatus was observed in many tumor cells. The hyaloplasm was characterized by quite a few osmiophilic fat droplets and vacuoles with microvilli (which may mean the latter may have originated from folds of the cell membrane). Virus-like particles (corresponding in part to Bernard's "A" and "C" type) of 45-200 mμ in diameter were detected in the cytoplasm with 50-80 mμ particles in the nucleus of certain tumor cells. The most significant finding was the intranuclear localization of virus-like particles, seen for the first time in a growth other than Ehrlich ascites carcinoma or tumors due to polyoma virus.

- 64-229 FAILURE TO SHOW CARCINOGENICITY OF THE HYDROCARBONS 5α- AND 5β-ANDROSTANE. (E.) Segaloff, A. (Alton Ochsner Med. Found., New Orleans, La.) and R. H. Coleman. Steroids 3(2):215-217, 1964.

CFW mice or Fischer rats (both weanling females, in groups of 10) were given 5α- or 5β-androstane (25 or 100 mg, in steroid suspending vehicle, s.c.). All except 2 control animals survived more than 1 yr. and 9 survived more than 2 yr. The only tumors in the mice were 2 non-transplantable mammary adenocarcinomas in controls. While no tumors developed in rats, small nodules

were found which contained 5β -androstande crystals in a benign stroma.

- 64-230 INFLUENCE OF AGE ON SUSCEPTIBILITY TO LIVER CARCINOGENESIS AND SKIN INITIATING ACTION BY URETHANE IN SWISS MICE. (E.) Chieco-Bianchi, L. (Inst. Anat. Path., U. Bari, Italy), G. De Benedictis, G. Tridente and L. Fiore-Donati. *Brit. J. Cancer* 17(4):672-680, 1963.

Swiss mice of both sexes inj. s.c. within 24 hr. of birth with a total of 2 mg of urethan (U) when killed at 180, 240, 300, 360, 420 and 480 days showed the following number of hepatomas (male and female), resp.: 1/20, 0/20; 2/17, 0/12; 5/18, 0/16; 11/20, 0/23; 13/15, 2/22; 17/23, 2/25 (controls 19/227, 4/222 after 360-720 days). High incidence of hepatomas occurred only in males. In mice which received U (1 mg/g s.c.) at ages 5, 20 and 40 days and killed after 420 days, hepatoma incidence (male and female) was, resp.: 9/13, 2/11; 1/13, 0/16; 0/11, 0/9. High hepatoma incidence was seen chiefly in males inj. at 5 days. Among other tumors seen, were pulmonary adenomas, lymphomas, mammary tumors, tumors of the uterus, ovary and forestomach; skin papillomas and nonmalignant vascular lesions were also observed. Newborn and adult mice given U (1 mg/g s.c.) and percutaneous treatment with croton oil (0.05 ml, 50% soln. in paraffin oil) after 40 days and continued for 10 mo. showed papillomas in 26/59 (44%) in newborn mice and 8/41 (19.5%) in 40-day-old animals with approx. the same latent periods. Lactating mothers were given U (30 mg, intragastric) on the 1st, 3rd and 5th day after parturition. The mice in one group of litters which were painted with croton oil at age 40 days for a 10-month period, developed tumors in 8/44 (18%); av. latent period was 122 days. In croton oil only controls tumors developed in 30/712 (4.2%). Grossly, the tumors appeared as sessile or pedunculated papillomas with 4/5 tumors localized in the posterior portion of the back.

- 64-231 THE CATABOLISM OF URETHAN BY MOUSE-LIVER HOMOGENATES. (E.) Mirvish, S. S. (Dept. Exptl. Biol., Weizmann Inst. Sci., Rehovoth, Israel) and A. M. Kaye. *Biochim. Biophys. Acta* 82(2):397-399, 1964.

When the rate of catabolism of urethan (U) was studied in relation to its carcinogenic effect, it was previously reported that mouse liver homogenates metabolized carbonyl-labeled (C^{14})-U to $C^{14}O_2$ in low yields, but the present study indicates that a C^{14} -containing impurity in the commercially obtained C^{14} -U was the substrate responsible for the greater part of the previous activity. Fresh liver homogenates and slices had weak but definite enzymic activity towards C^{14} -U purified by recrystallization. Inhibition studies indicate that esterases are involved in U catabolism.

- 64-232 THE EXPERIMENTAL PRODUCTION OF VASCULAR TUMOURS IN THE RAT. (E.) Howell, J. S. (Dept. Path., U. Birmingham, England). *Brit. J. Cancer* 17(4):663-671, 1963.

When 1-day-old laboratory stock albino rats were admin. 9,10-dimethyl-1,2-benzanthracene (1.2 mg in olive oil, s.c.), multiple hemangiomas developed in 41/93 (44%) of the survivors. Av. induction times in the 19 female and 22 male tumor-bearing rats were 319 and 358 days, resp. Soft tissue and s.c. hemangiomas were classified histologically as follows: 21 benign (capillary and cavernous type), potentially malignant (22 hemangio-endotheliomas, 3 hemangiopericytomas), 4 malignant (hemangiosarcomas). The potentially malignant hemangio-endotheliomas presented cells and nuclei with considerable variation in size and shape, arranged within the reticulin network and the channels formed by it. The hemangiopericytomas presented proliferating cells outside and in the interstices of a more complex reticulin network without channels. The malignant hemangiosarcomas presented very pleomorphic appearances with variation in cell size and shape, with tumor giant cells and aberrant mitotic figures.

- 64-233 AZO-DYE CARCINOGENESIS: RIBONUCLEOTIDES AND RIBONUCLEASES. (E.) Noddes, J. T. (Dept. Appl. Biol., Brunel Coll., Acton, London W.3) and E. Reid. *Brit. J. Cancer* 17(4):745-774, 1963.

Livers of 7-week-old male Institute albino strain rats fed various azo dyes (a 20% protein diet containing 0.075% dye) showed the following histologic appearances after 35 days: bile duct hyperplasia, fibrosis and fat deposition in 3'-methyl-dimethylaminoazobenzene (3'-Me-DAB)-fed rats; normal except for limited bile-duct hyperplasia and necrosis in 4'-fluoro-DAB-fed rats; normal in those fed 2-methyl-DAB and 4'-methyl-DAB. Nodules induced by prolonged feeding (90-110 days) of 3'-Me-DAB were investigated after 7-12 mo. and classified mostly as hepatomas (with varying areas of limited, fairly extensive and very extensive necrosis) and "hyperplastic nodules" (few hepatic cells, little necrosis, sometimes resembling cholangiomas). When 4'-methyl-DAB was fed to 4 rats for 137 days, the livers were normal on autopsy at 15 mo. The activities of glucose-6-phosphatase (G-6-Pase) decreased in the dye-induced nodules, while the activities of G-6-P dehydrogenase showed increases in both nodules and precancerous liver. High uridine-5'-monophosphate (UMP) and UTP levels were revealed early in azo dye feeding, but except for somewhat high UDP values, the uridine nucleotide levels were often normal. Fibrotic nodules showed rather low UTP, UDP glucose, UDP glucuronate and UDP acetylglucosamine levels. Purine nucleotides were low in both precancerous liver and nodules. Consistent decreases in adenosine diphosphate (ADP), guanosine DP and inosine monophosphate were noted and, for precancerous liver, correlated with the carcinogenicity of the dyes. Pyridine nucleotides except nicotinamide adenine dinucleotide (NAD),

ended to diminish in precancerous liver and some of the nodules; early decreases in NADP and NADPH₂ are correlated with carcinogenicity. Decreases in UDP glucuronate and NADPH₂ in the nodules seemed significant, when compared to results in non-tumor hepatomas and in published reports. A marked rise appeared in the acid RNase activity of supernatant fractions after 1 wk. of 3'-Me-DAB treatment. Altered phosphodiesterase activity towards certain cyclic mononucleotides was seen in mitochondrial or microsomal fractions from cancerous liver and nodules.

234 THE USE OF RAT BLADDER POUCHES TO ELUCIDATE THE MODE OF ACTION OF A CHEMICAL WHICH INDUCES HYPERPLASIA IN THE BLADDER EPITHELIUM. (E.) Santana, S. (Hosp. U. Bahia, Salvador, Bahia, Brazil). Brit. J. Cancer 14(4):715-718, 1963.

10 adult female Sheffield rats isolated bladder pouches were devised leaving the bladder as a non-functional organ. When the pouch was viable, thylsulfonynaphthalene-1-sulfonamide (18 mg/ml of arachis oil 6 days/wk. x 2 p.o., total dose 216 mg) was admin. and 6-8 wk. after operation, varying degrees of mild to severe epithelial hyperplasia were seen in the main bladder but not in the pouches. Edema of the subepithelial tissues was seen and mild inflammatory exudate occurred in 3 bladders. In untreated controls, hyperplasia of the pouch near the loop occurred in 2/9, while bladder hyperplasia occurred in 1/9. The data indicate that the agent acts via the urine rather than via the blood stream.

235 THE ACETYLATION OF TESTOSTERONE BY RAT AND MOUSE MAMMARY TISSUE. (E.) King, J. B. (Imperial Cancer Res. Fund, Lincoln's Fields, London, W.C.2), J. Gordon and J. A. H. J. Endocr. 28(3):345-346, 1964.

Experiments on the metabolism of C¹⁴-4-testosterone by the mammary gland of pregnant rats and mammary tumors induced with dimethylbenzanthracene, the formation of a minor metabolite with the same chromatographic behavior as testosterone acetate was indicated. A similar compound was found in the mammary gland of pregnant mice and in spontaneous mammary tumors in mice.

236 MOUSE LIVER REGENERATION IN THE PROCESS OF EXPERIMENTAL CARCINOGENESIS. (E.) Shteyn, V. I. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci., Moscow). Fed. Proc. 23(2):T358-T361, 1964.

English translation of the Russian paper previously abstracted as CRA 1(4):#655, 1963.

237 CHANGES IN RAT SUBCUTANEOUS CONNECTIVE TISSUE CAUSED BY SMALL DOSES OF 7,12-DIETHYLBENZ- α -ANTHRACENE. (E.) Vasil'ev, Iu. M.

(Inst. Exptl. Clin. Oncol., USSR Acad. Med. Sci., Moscow). Fed. Proc. 23(2) (Pt. 2):T362-T364, 1964.

An English translation of the Russian paper previously abstracted as CRA 1(1):#86, 1963.

64-238 FLUORESCENCE OF CHICKENS AND EGGS FOLLOWING THE FEEDING OF BENZPYRENE CRYSTALS. (E.) Rigdon, R. H. (Dept. Path., U. Texas Med. Br., Galveston) and J. Neal. Texas Rep. Biol. Med. 21(4):558-566, 1963.

3,4-Benzpyrene (BP) in a benzene-flour mixture added to chick food (Startena) in conc. of 0.01-0.5 mg/g of food shows a blue fluorescence in ultraviolet light; Startena alone shows none. The skin, feathers, gallbladder and viscera of 1-day-old White Rock chicks 6 days after feeding with 0.1 and 0.5 mg BP showed blue fluorescence, while chicks fed 0.01 mg BP showed faint blue fluorescence in skin, but not in the gallbladder. Chicks fed control mixture without BP showed minimal or no fluorescence. The blue fluorescence decreased rapidly after BP was discontinued. Similar fluorescence findings were observed after 30 days. The gain in wt. in a 30-day period was the same for BP-fed and control-fed chicks. No deaths occurred. Shells from eggs of the control group fluoresced red, while those of BP-fed (0.25 and 1.0 mg/g food) chicks fluoresced a bluish-pink. BP-fed yolks showed a yellow-white color as compared to the deep yellow of control yolks after 40 days. No differences were observed in egg whites. Experiments on the effect of different conc. of BP/g of food on the fertility of eggs did not give conclusive results: there were 0/50 fertile eggs in hens receiving 0.25 mg BP; 35/39 fertile eggs with the control diet; 41/42 in hens receiving 1.0 mg BP. The present study gives no evidence of BP-induced changes in either sperm or ovum. Adult BP-fed chickens are now under observation for neoplasms. (For a similar study on rats, see CRA 2(2):#239, 1964.)

64-239 EFFECT OF FEEDING BENZPYRENE ON REPRODUCTION IN THE RAT. (E.) Rigdon, R. H. (Dept. Path., U. Texas Med. Br., Galveston) and E. G. Rennels. Experientia 20(4):224-226, 1964.

No significant differences were noted in the ovarian cycles, ovulation, fertilization or implantation of 90-day-old female rats fed lab chow containing 3,4-benzpyrene (BP; 1 mg/g of food) compared to controls. After mating, 3 control group rats gave birth to litters of 3, 6 and 11 grossly normal rats (1 was either stillborn or died soon after delivery). Of 5 females fed BP during gestation, only 1 reached term and delivered 4 young: 1 malformed stillborn, 1 normal stillborn and 2 live young. One of these was killed while the other died after 3 days from starvation, since the mother showed no signs of lactating. Autopsies of 2 BP-fed females mated to BP-fed males revealed fetal resorption in 1 rat, while the other had 4 dead fetuses in the uterine horns.

The pregnant controls showed 10 living and normal fetuses in the uterine horns. When observed with UV light the uterine wall, placenta, fetal membranes and young of BP-fed rats fluoresced blue, while the placenta from a normal rat had a red fluorescence. No tumors were observed and no significant differences were noted in the ovaries, adrenals or pituitary glands of control and BP-fed females. (For similar studies on chicks, see CRA 2(2):#238, 1964.)

- 64-240 CHANGES IN EPITHELIAL CELL LYSOSOMES DURING EXPERIMENTAL ORAL CARCINOGENESIS. (E.) Smith, C. J. (Dept. Dent. Sci., Royal Coll. Surg. England, London, W.C.2) and G. E. Camilleri. *Nature (London)* 201:512-514, 1964.

When the cheek pouches of 6-8-week-old female Golden Syrian hamsters were painted with 9,10-dimethyl-1,2-benzanthracene (0.5% soln. in paraffin 3x/wk.), papillomas appeared within 8 wk. and malignant tumors within 12 wk. of treatment. The lysosomes of malignant epithelial cells from frozen sections of squamous cell carcinoma and smears of exfoliated cells from malignant lesions were of increased size and to some degree had lost the discrete pattern characteristic of the normal cell. A biopsy of human oral carcinoma, treated in the same way, showed a similar change in lysosomes. It appears that the appearance of lysosomes in epithelial cells may prove to be of diagnostic value in assessing malignancy.

- 64-241 TOXIC EFFECTS OF GROUNDNUT MEAL CONTAINING AFLATOXIN TO RATS AND GUINEA PIGS. (E.) Butler, W. H. (University Coll. Hosp. Sch. Med., London, W.C.1) and J. M. Barnes. *Brit. J. Cancer* 17(4):699-710, 1963.

The diets of rats and guinea pigs contained toxic groundnut [peanut] meal (TGM) which, itself, had varying proportions of aflatoxin (AF; toxic metabolites of the fungus *Aspergillus flavus*). Control animals fed up to 50% nontoxic groundnut meal showed no adverse effects. Among rats continuously fed TGM (40-50%, 2.8-4.0 ppm AF), 3/6 which survived 35-38 wk. showed undifferentiated hepatocarcinomas, 2/6 partially differentiated tumors. Of six male rats fed 50% TGM, 3.5-4.0 ppm AF for 16 wk. and then returned to a normal diet, 4 showed hepatocarcinomas, and 2 had multiple atypical regenerative nodules in the liver. Of a group of male and female rats fed 20% TGM (1.4-1.6 ppm AF) for 12 wk., 5/7 (38-73 wk.) had solid white liver tumors; among a second group fed the same diet for 26 wk., 9/10 (40-58 wk.) had distorted livers with both solid tumors and large cystic spaces, 1/10 had an adenocarcinoma of the stomach, 1/10 had renal adenoma, 2/10 had large cholangiocarcinomas. Of female rats fed 10% TGM (0.7-0.8 ppm AF) continuously, 5/6 (67-82 wk.) had solid liver tumors (necrotic and hemorrhagic). Among 5 surviving female rats fed 5% TGM (0.35-0.5 ppm AF) continuously, there occurred 5 carcinomas (stomach 2, salivary gland 1,

lacrimal duct 1, lung 1) and 2 undifferentiated hepatocarcinomas. In all the experiments with rats, a total of 13 metastases were found. In male and female guinea pigs fed 5, 10 or 20% TGM continuously, while definite liver changes were observed, no carcinogenic effects were reported.

- 64-242 EFFECT OF TRANSPLENTAL MITOTIC INHIBITORS ON THE FETAL HAMSTER EYE. (E.) Ferm, V. H. (Dept. Path., Dartmouth Sch. Med., Hanover, N.H.). *Anat. Rec.* 148(2): 129-133, 1964.

The consistent appearance of such congenital malformations as microphthalmia and anophthalmia in the hamster eye (see CRA 1(8):#1515, 1963) following i.v. inj. of colchicine (C), vinblastine (VLB) and vincristine (VCR) led to studies on their comparative mitotic-arresting activity on the lens and retina of the fetuses of pregnant hamsters inj. i.v. with C (5-50 mg/kg), VLB (0.25-2.5 mg/kg) and VCR (0.1-2.5 mg/kg) at day 14 of gestation with fetus recovery 3 hr. later. Examination of lens and retina sections revealed a marked metaphase arrest with C at 10 mg/kg, corresponding to its most effective teratogenic dose. The mitotic arrest level with VLB and VCR was not as striking, although there was increased mitotic arrest in these tissues; there was no apparent correlation of the peak of mitotic arrest with suggested teratogenic levels of these compounds. The natural resistance of golden hamsters to C does not appear to be manifest in developing embryos in utero.

- 64-243 THE EXPERIMENTAL PRODUCTION OF PRECANCER AND CANCER OF THE STOMACH. (E.) Solov'ev, A. A. (Inst. Norm. Path. Physiol., Acad. Med. Sci., USSR), E. D. Klimenko, N. A. Nilova and O. M. Pozdnyakov. *Bull. Eksp. Biol. Med. (N.Y.)* 55(1):73-76, 1964.

An English translation of the Russian paper previously abstracted as CRA 1(1):#85, 1963.

- 64-244 POLYCYTHEMIA VERA FOLLOWING TREATMENT OF MEGALOBlastic ANEMIA WITH FOLIC ACID. (E.) Grønbaek, P. (Med. Dept. F, Frederiksborg County Hosp., Hillerød, Denmark) and J. V. Larsen. *Acta Med. Scand.* 174(6):781-784, 1963.

A case is reported of a 55-year-old woman who developed megaloblastic anemia when treated with the anticonvulsive drug phenytoin, and who later developed polycythemia vera during treatment with folic acid. The deficiency of folic acid utilization was demonstrated by formiminoglutamic acid (FIGLU) tests, which showed falling values during admin. of folic acid. Besides RBC, WBC and platelet studies, the polycythemia vera was verified by radioactive sodium chromate blood-vol. studies. No evidence of polycythemia was found before the treatment with anticonvulsive drugs, vitamin B12 and folic acid.

4-245 DEMONSTRATION OF CARCINOGENIC HYDRO-CARBONS, WITH SPECIAL REFERENCE TO PAPER CHROMATOGRAPHY. (Ger.) Pietzsch, A. City Hosp., Dresden-Friedrichstadt, Germany). Arch. Geschwulstforsch. 21(2):137-143, 1964.

Analytical methods for the detection of hydrocarbons are reviewed; ascending column paper chromatography is considered the most reliable technique for this purpose. Details of the method used by the author (choice of solvents, pre-treatment of paper, calculation of Rf values) are described. Detection of the chromatographic spots by means of color reactions was found unsatisfactory; fluorometry proved to be the method of choice. With this technic, detection of 3,4-benzpyrene in quantities as low as 0.004 µg was possible. The ratio of polycyclic aromatic hydrocarbons in tobacco smoke was found to be as follows: A:B:C:D:E = 2:3:4:5:6 (A = anthracene, fluorene, 1,2-benzanthracene, 1,2-dibenzanthracene; B = perylene; C = fluoranthene, 9,10-dimethyl-1,2-benzanthracene, 1,2-benzpyrene; D = pyrene; E = phenanthrene, 3,4-benzpyrene).

4-246 THE EFFECT OF NORMAL LIVER POLYPEPTIDE EXTRACTS ON THE GROWTH OF 3,4-BENZ-PYRENE SARCOMA IN THE RAT. (It.) Modica, F. Inst. Gen. Path., U. Bari, Italy) and P. De Nardis. Atti Acad. Pugliese Sci., Bari (Nuova Serie) 19(Pt. 2):365-378, 1961.

40 albino rats of both sexes, av. wt. 200 g, receiving s.c. into the interscapular region 1 mg of 3,4-benzpyrene (BP; 0.5% in acid-free almond oil) every 20 days for 3 inj., the simultaneous admin. of normal liver polypeptide extracts (10 mg/kg/2 days, i.m., continued for 20 days after the third dose of BP or until death of the animal) did not affect the development of BP-induced sarcomas, the latency period, or the survival time after the tumor appeared. Treatment begun at time of tumor appearance and continued until death was equally ineffective.

4-247 STUDIES ON THE CHANGE OF 20-METHYLCHOLANTHRENE, ONE OF CARCINOGENIC HYDROCARBONS IN THE BODY. 5. THE INTRACELLULAR DISTRIBUTION IN LIVER CELLS OF 20-METHYLCHOLANTHRENE ADMINISTERED *IN VIVO*. (Jap.) Sasaki, K. Dept. Biochem., Tokushima U. Sch. Med., Japan). Shikoku Igaku Zasshi (Shikoku Acta Med.) 19(6):343-488, 1963.

Immediately after admin. of 20-methylcholanthrene (MC; 50 mg dissolved in horse serum, i.v.) to rabbits the carcinogen was found in all fractions of liver studied: nuclei, mitochondria, microsomes and supernatant, especially those of the nuclei and mitochondria. After 3 wk. the amount of MC in the microsomes and supernatant was extremely small and a large portion remained in the nuclei and mitochondria; 61.5% of the total

liver MC was in the nuclei and 29% in the mitochondria.

64-248 SUCCESS IN CELL-FREE TRANSPLANTATION OF 20-METHYLCHOLANTHRENE-INDUCED RF MOUSE LEUKEMIA. (Jap., Abstract) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino, T. Sezaki and M. Suzuki. Nippon Ketsueki Gakkai Zasshi (Acta Hemat. Jap.) 26(3,4):388-389, 1963.

See CRA 1(8):#1467, 1963, ibid., 1(9-10):#1702 and ibid., #1758, 1964.

64-249 DISTRIBUTION OF METHYLCHOLANTHRENE IN ORGANS OF 20-METHYLCHOLANTHRENE-INDUCED RF MOUSE LEUKEMIA. (Jap., Abstract) Sezaki, T. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino and M. Suzuki. Nippon Ketsueki Gakkai Zasshi (Acta Hemat. Jap.) 26(3,4):392, 1963.

In a study of 20-methylcholanthrene (MC)-induced leukemia in the RF mouse (see CRA 2(2):#248, 1964), those with the myeloid type showed invasion first in the bone marrow and spleen; in those with the lymphoid type invasion occurred first in the spleen, lymph glands or thymus. Later invasion gradually spread to other organs. In a study of distribution, higher conc. of MC were found in the thymus, bone marrow, spleen, lymph nodes and liver of those mice with myeloid leukemia than in those with lymphoid leukemia. While MC did not induce leukemia in the C3H strain, carcinogen distribution in the body was similar to that in the RF strain.

64-250 MORPHOLOGIC AND IMMUNOELECTROPHORETIC STUDY OF INDUCED PLASMOCYTIC TUMORS IN MICE. (Fr.) Hermann, G. (Inst. Sci. Cancer Res., Villejuif, Seine, France). C.R. Acad. Sci. (Paris) 257(25):4071-4074, 1963.

Following repeated i.p. inj. of Bayol F (an aromatic-free mineral oil) into 120 Balb c/Gif mice, mononucleated cells (basophilic) and macrophages appeared during the first days (stage I) in the peritoneal cavity. A short time after the inj., 100% of the animals developed multinodular paraffinomas (stage II) with nodules rich in basophilic and hyperbasophilic monocytes, macrophages, and normal plasmocytes. In the course of repeated inj., while the paraffinomas continued to grow, the immunoelectrophoretic picture revealed an increasing heterogeneity of γ-globulins. Ten mo. after the first inj., hemorrhagic and plasmocytic ascites appeared in 44% of the mice and tumors in 13% (stage III); the tumors were often isolated and localized in the mesentery. Serum protein changes appeared often shortly after the development of ascites and tumors, but the immunoelectrophoretic picture was inconclusive as to the presence of a tumor. In a further series of experiments, the development of paraffinomas appeared to be dependent upon the amount of Bayol F

admin. and the frequency of the inj. regardless of the age of the mouse. The appearance of stage I and II could be stimulated but the formation of the tumor itself appeared to be due to a spontaneous transformation. Particularly interesting was the case of a mouse with a multiple tumor (a sarcoma) with 3 different localizations in the mesentery; the immunoelectrophoretic picture revealed the presence of a myelomatous protein in the serum and especially in the ascites fluid. This tumor became transplantable with 100% of "takes" after 4 passages; the myelomatous γ -globulin appeared in the host generally 8-14 days after inoc.

- 64-251 MALIGNANT DEGENERATION OF EXPERIMENTAL URETHAN-INDUCED PULMONARY ADENOMA IN SWISS MICE. I. HISTOLOGIC STUDY. (Fr.) Driessens, J. (Dept. Cell. Biol., Inst. Cancer Res., Lille, France), A. Clay, J. Vanlerenberghe, L. Adenis and P. Quandalle. *C.R. Soc. Biol. (Paris)* 157(7):1448-1449, 1963.

See CRA 1(9-10):#1685, 1964.

- 64-252 AN INTERESTING HYPOTHESIS ON THE MECHANISM OF ACTION OF CARCINOGENIC COMPOUNDS THROUGH INTERFERON. (Fr.) De Maeyer, E. (Dept. Virol., Rega Inst., U. Louvain, Belgium) and J. De Maeyer-Guignard. *Med. Hyg. (Geneve)* 21(611):852, 1963.

The results of experiments conducted with 7,12-dimethyl-1,2-benzanthracene (DMBA) are in agreement with those obtained with 20-methylcholanthrene (MC) and described in CRA 1(6):#1145, 1963. Both MC and DMBA (0.01-0.1 μ g/ml) have been proved to inhibit the formation of interferon in tissue cultures (DE7R cells infected with Sindbis virus) and to stimulate viral growth *in vivo*. A new possible mechanism for the activity of a chemical carcinogenic compound may therefore consist in the inhibition of interferon synthesis resulting in the activation of a latent oncogenic virus.

- 64-253 ON THE ISOLATION OF CARCINOGENIC NUCLEIC ACIDS FROM TRANSPLANTABLE POLYOMA TUMORS OF RATS AND HAMSTERS. (Ger.) Graffi, A. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin), J. Gimmy and F. Schneiders. *Acta Biol. Med. German.* 12(1-2):219-221, 1964.

DNA and RNA were prepared from polyomas of rats and hamsters which were produced 3 yr. previously by inoc. of BBT₂ virus. The ultrafiltrates of starting materials for nucleic acid production (filtrates of BBT₂ rat and hamster tumors) were practically devoid of carcinogenic activity (1/246 and 2/103, resp.). The isolated tumor DNA produced 8 characteristic tumors in 7/29 rats; 3 other, etiologically unrelated tumors (1 epithelioma and 2 mammary adenofibroma),

appeared in 3 other rats. The RNA preparations were not carcinogenic (0/35).

- 64-254 COMPLEXES OF CARCINOGENIC HYDROCARBONS WITH PROTEIN AND DNA. (E.) Gemant, A. (Res. Lab., Grace Hosp., Detroit, Michigan). *Grace Hosp. Bull.* 42(1):17-28, 1964.

Polynuclear hydrocarbons are shown to complex with protein (human beta globulin, fraction III) and nucleic acids (sodium desoxyribonucleate) with an affinity directly related to their carcinogenicity. These *in vitro* studies were made on 3,4-benzpyrene, 1,2-benzanthracene and anthracene by measuring the conc. of the complexes using optical density. The minimum-complexing-globulin conc. for these hydrocarbons at 15 mg/100 ml were 10, 20 and 50 mg/100 ml, resp., producing the protein:hydrocarbon ratios of 0.7, 1.3 and 3.3. The minimum complexing DNA conc. with the hydrocarbons at 15 mg/ml were 10, 100 and 500 mg/100 ml, resp., producing ratios of 0.7, 6.6 and 33.3, resp. While the complexes with nucleic acids were less stable than those with globulin, the affinity remains related to carcinogenicity. Measurement of the 10-day percentage residual complexes with DNA indicates that the strength of binding is also increased with increasing carcinogenicity. These hydrocarbons have been shown to displace cholesterol from its complex with globulin or DNA. It is possible that the physicochemical changes of DNA produced by this hydrocarbon complexing might affect template replication in such a way as to produce malignancy. (See CRA 1(4):#761, 1963.)

- 64-255 TRANSILLUMINATION OF THE RAT URINARY BLADDER: AN AID IN TUMOR INDUCTION STUDIES. (E.) Veenema, R. J. (Dept. Urol., Columbia U. Coll. Physicians Surg., New York), B. Fingerhut and T. Pinzas. *Invest. Urol.* 1(5):425-428, 1964.

Female rats (Fisher 344) were fed a bladder carcinogenic diet (deficient in vitamin B₆ (pyridoxine) and containing N-2-fluorenylacamide (2-FAA)). Under anesthesia, the bladder was extended through a small incision and viewed in a darkened room with a no. 8 McCarthy panendoscope light source held posterior to it. After 5 mo. of the 2-FAA diet, the serosal vessels of the bladder were more tortuous and dilated, hyperemia was marked at the bladder dome and a small dark area of early tumor formation was noted; after 8 or 9 mo., a large, mature tumor filled the bladder dome, and the bladder wall appeared to be slightly thickened.

- 64-256 CARCINOGENICITY OF 3-METHYL-2-NAPHTHYLAMINE. (E.) Shenoy, K. P. (Indian Cancer Res. Ctr., Bombay, India), R. Y. Ambaye and T. B. Panse. *Curr. Sci.* 33(2):45-46, 1964.

male Swiss 12-14-week-old mice (8) were inj. s.c. with 3-methyl-2-naphthylamine (MeNA; 0.1 ml of a 3% soln. 2x/wk.) or 2-naphthylamine (NA; as above, both in refined groundnut oil); a control group received 0.1 ml of groundnut oil (2x/wk. s.c.). Animals treated with MeNA developed palpable fibrosarcomas (shown histologically) after an av. latent period of 120 days and the tumor incidence was 87.5%, while no tumors developed in the controls and in animals treated with NA. The fibrosarcomas were successfully transplanted into mice of the same strain. When 8 female 10-week-old Wistar rats were inj. s.c. with MeNA (3% soln. in refined groundnut oil, 5 mg/100 g 2x/wk.), palpable carcinomas (shown histologically) developed in all the animals after an av. latent period of 126 days. The carcinomas were successfully transplanted into rats of the same strain. The results indicate that MeNA is a potent and direct carcinogen and is in fact more dangerous than NA.

4-257 STUDIES ON THE NEWT TEST FOR CARCINOGENICITY. 4. SUPPLEMENTARY EXPERIMENTS ON SPECIFICITY. (E.) Arffmann, E. (Dept. Path., Finsen Inst., Copenhagen, Denmark). *Acta Path. Microbiol. Scand.* 60(1):13-26, 1964.

The specificity of the newt (*Triton cristatus*) test when applied to polycyclic hydrocarbons has been confirmed in supplementary experiments showing complete inactivity of anthracene (0.1 and 0.5% soln.) and triphenylene (0.5% soln.) and weak reaction to 3',6-dimethylbenz[a]anthracene (0.00625-0.025% soln.) as compared to dibenz[a,h]anthracene in the same low conc. (see CRA 1(8):#1519, 1963). Quantitative experiments with benz[a]anthracene and chrysene support the conclusion that the degree of response parallels the conc. of the test soln. The negative reaction to 1,2,4-trimethylphenanthracene persisted after raising the conc. to 1%. Arsenic trioxide dissolved in water or suspended in peanut oil is negative; isonicotinic acid hydrazine in oily suspension induced a weak reaction. Two alkylating agents, diethylnitrosamine and N-nitroso-N-methylurethan, had a moderate effect in oily soln.; diethylnitrosamine was inactive in water. The last-named four carcinogens represent at least two groups of quite different chemical structures, which also differ essentially from polycyclic hydrocarbons. Yet the results in *Triton cristatus* are in reasonable concordance with results in mammals and strongly suggest that the positive conclusion as to the specificity of the newt test may be extended to chemical compounds other than the polycyclic hydrocarbons, at least if given in oil.

4-258 MORPHOLOGY OF EXPERIMENTAL BRAIN TUMOURS. (E.) Schiefer, B. *Acta Neurochir. (Wien)* (Suppl. 10):57-67, 1964.

see CRA 1(2):#205, 1963.

64-259 ULTRASTRUCTURAL CHANGES IN THE RAT LIVER PRODUCED BY N-2-FLUORENYLDIACETAMIDE.

(E.) Mikata, A. (Dept. Anat. Path., Washington U. Sch. Med., St. Louis, Mo.) and S. A. Luse. *Am. J. Path.* 44(3):455-479, 1964.

The hepatic ultrastructures were compared using 2 groups of 15 Buffalo strain male rats: the controls were on a basal diet and the experimental animals received in addition 0.1% N-2-fluorenyldiacetamide (av. daily intake was 4.2 g/rat). When observed over periods of 1 up to 30 days with both the electron and light microscope, the hepatic cells of the treated rats exhibited several changes: increase in bulk of smooth-surface and decrease in rough-surface endoplasmic reticulum (day 14) with a concomitant loss of its parallel arrangement, transient accumulation of glycogen which was depleted on day 23, appearance of dark and light cells with mitochondrial alteration in the latter, cytoplasmic vesiculation (day 14), finally, diffuse mitochondrial enlargement with cytoplasmic myelin figure formation (day 30). Ductular proliferation progressed until it involved much of the lobule. These early morphologic changes resemble those produced by other hepatic carcinogens: 3'-MeDAB, dimethylnitrosamine and diethylnitrosamine.

64-260 EFFECT OF CERTAIN POLYCYCLIC HYDROCARBONS ON THE INCORPORATION OF AMINOACIDS INTO SOLUBLE RIBONUCLEIC ACIDS. (E.)

Chang, M. (Dept. Chem., Baylor U., Waco, Texas) and T. J. Bond. *Nature (London)* 201:623, 1964.

The biochemical effects of 9,10-dimethyl-1,2-benzanthracene (DMBA) and 20-methylcholanthrene (20-Me) on the formation of aminoacyl-sRNA, and the effect of DMBA on the amino acid activating enzyme system, were described. The effect of DMBA on the C¹⁴-amino acid incorporation of glycine, glutamic acid and leucine into transfer RNA, resp., was 61.6%, 87.2% and 99.8% of the control (120.7, 127.4 and 148.9 cpm/mg, resp.), whereas with 20-Me, the incorporation was 79.2%, 80.4% and 116.2% of the control, resp. Enzyme fractions obtained from *E. coli* cells grown in the presence of 300 µg/ml suspensions of DMBA demonstrated approx. a 30% decrease in the ability to synthesize glycyl-sRNA with no decrease in the pH 5 protein synthesis over cells grown in the absence of this polycyclic hydrocarbon. This suggests that the observed effects of DMBA on glycine uptake arise from its effect on the enzyme system, not that on sRNA. The author indicated that the results of both experiments may be important in the examination of the overall mechanism of carcinogenesis by these chemicals.

64-261 ELECTRONMICROSCOPIC EXAMINATION OF AN EXPERIMENTALLY-INDUCED INTRACRANIAL SARCOMA IN THE ALBINO MOUSE. (Ger.) Wechsler, W. (Max Planck Inst. Brain Res., Cologne, Germany). *Acta Neuropath. (Berlin)* 3(2):119-136, 1963.

Eight mo. after intracranial implantation of a methylcholanthrene pellet (dose not stated) in a mature albino mouse, a resulting fibrosarcoma had broken through the skull and grown to the size of a walnut, under the skin. Conventional and electron-microscopic findings, which were typical, are reported in detail.

- 64-262 THE INFLUENCE OF SOME IRRITANT CHEMICALS AND SCARIFICATION ON TUMOUR INITIATION BY URETHANE IN MICE. (E.) Pound, A. W. (Dept. Path., Brisbane Hosp., Australia) and H. R. Withers. *Brit. J. Cancer* 17(3):460-470, 1963.

Male Hall mice, untreated or pretreated with 0.25 ml acetone (A) to half or all of the skin of the back, were inj. immediately or 12 hr.-6 days later with urethan (U; 25 mg s.c. between the scapulae) and subsequently painted with croton oil (C; x 1/wk. x 20). Among 12 such groups of 20 mice each, in which the effect of C and A was tested 0, 12, 18 or 24 hr. or 2, 4, 6 days before the inj. of U, the total number of tumors on the right side (54), midline (11) or left side (50) was not influenced by prior application of A. Various irritants--acetic acid 50%, cantharidin 0.1%, iodoacetic acid 1%, trichloroacetic acid 5% (all in 0.25 ml acetone) or undiluted xylene or vegetable turpentine (0.25 ml), or scarification--preceded by 1-6 days the inj. of U. The number of tumors in scarified mice or in those treated with an irritant was greater on the treated than on the untreated side. The effect in descending order for one group was xylene, acetic acid, turpentine; in another group, the order was cantharidin, iodoacetic acid, scarification and lastly trichloroacetic acid. The augmenting interval was significant if the interval between the preliminary application and inj. of U was 24 hr., reached a max. at 2 or 3 days and declined by day 5 or 6. The augmenting effect was related to the severity of the local effect of the treatment on the skin.

- 64-263 AN ATTEMPT TO DEMONSTRATE AUTOLOGOUS RECOGNITION OF MALIGNANT CELLS BY AN IN VIVO SYSTEM. (E.) Anderson, M. R. (Dept. Exptl. Path., U. Leeds Sch. Med., England). *Nature (London)* 201:202, 1964.

In an attempt to demonstrate autologous recognition of malignant cells by an *in vivo* system, fibrosarcomas were induced in Sheffield Wistar rats by 20-methylcholanthrene (MC; 0.05 g s.c. into the anterior abdominal wall). The tumor was removed and a small part enclosed in a "Millipore" chamber was inserted into the host's peritoneal cavity for 8-12 days. Cell suspensions of the rat host spleen and the stored original tumor (4:1 ratio) were then inj. s.c. into 1 flank of guinea pigs; the other flank of each was inj. with normal spleen + tumor cells and served as controls. When the flares under the skin were examined 3-4 days later, the flares were predominantly larger in 33/43 of the experimental

flanks as compared to the controls (larger in 2/43). Animals treated as above with autologous tumor-sensitized spleen and tumor cells showed larger flares in 24/34 as compared to control flanks inj. with autologous tumor-sensitized spleen and with autologous liver cells as antigen (larger 3/34). In 3/4 guinea pigs inj. with autologous liver-sensitized spleen and liver cells, the flare was larger than control flanks inj. with an empty "Millipore"-sensitized spleen and liver cell (1/4). It was noted that there appears to be a specific sensitization of the spleen to autologous tumor cells.

- 64-264 EXPERIMENTAL RHABDOMYOSARCOMAS IN RATS AND GUINEA PIGS. (It.) Maltoni, C. (Inst. Gen. Path., U. Bologna, Italy), R. Laschi and C. Cavina. *Tumori* 49(5):315-339, 1963.

Subcutaneous rhabdomyosarcomas were induced in 6/8 26-week-old, male guinea pigs surviving a single, 5 mg, s.c. inj. of 9,10-dimethyl-1,2-benzanthracene (DMBA), with a mean latent period of 50 wk.; and in 4/10 guinea pigs which received 5 mg of 20-methylcholanthracene (MC), with a mean latent period of 48 wk. Similar doses of 3,4-benzpyrene (BP) and 1,2,5,6-dibenzanthracene (DB) were fatal to all the treated animals before tumors had time to develop. In 21-week-old, male, albino rats, the same dose of DMBA induced tumors in all surviving animals, with a mean latent period of 17-24 wk.; in females of the same age and strain, tumor incidence was 25/37, with a mean latent period of 21 wk. Doses of 3 mg of DMBA induced tumors in 4/4 surviving 21-week-old males, 3/5 surviving 4-week-old males, and 2/2 surviving 98-week-old males; mean latent periods were 26 wk. in each case. Doses of 5 mg of MC, BP, and DB proved fatal to 21/21, 20/21, and 20/21 21-week-old males, resp., before tumors could develop. Tumors appeared in the 2 survivors after a latent period of 13 and 35 wk., resp. The authors point out that experimental induction of rhabdomyosarcomas in rats has been reported previously (although not with such high incidence), but that this type of tumor has not been reported previously in the guinea pig.

- 64-265 EFFECT OF DEOXYRIBONUCLEIC ACID FROM NORMAL LEUKAEMIC LYMPHOID TISSUE ON THE INCIDENCE OF LEUKAEMIA IN (AKR x C3H)_{F1} HYBRID MICE. (E.) Hays, E. F. (Dept. Biophys., U. California Sch. Med., Los Angeles) and J. A. Carr. *Nature (London)* 201:780-781, 1964.

Effects of s.c. inj. of 0.1 ml of freshly prepared DNA soln. containing 400-1,000 µg/ml from normal and leukemic lymphoid tissue were studied in groups of 24-72 hr. old (AKR x C3H)_{F1} hybrid mice. In mice given DNA from pooled normal spleen and thymus of 4-6-week-old C3H or AKR mice, combined incidence of leukemia (always lymphocytic) was 64% of 25 females, 41% of 17 males (combined, 55%); the leukemias developed within 7-14 mo. (mean age 10 mo.). In those given "leukemic"

DNA (spleen, lymph nodes or thymus of AKR mice with spontaneous leukemia) incidence of leukemia was 58% of 24 females, 70% of 10 males (combined 62%); age of onset was 6.5-14 mo. (mean, 10 mo.). Incidence in non-injected littermate controls was 72% of 43 females, 33% of 42 males (combined 53%). Judged as a whole, there was no significant difference in the incidence of leukemia. The high incidence in the treated males is of doubtful significance since only 10 mice were involved.

4-266 CONCENTRATIONS AND RATES OF SYNTHESIS OF NICOTINAMIDE-ADENINE-DINUCLEOTIDE PHOSPHATE IN PRECANCEROUS LIVERS AND HEPATOMAS INDUCED BY AZO-DYE FEEDING. (E.) Clark, J. B. (Dept. Biochem., University Coll., London), L. Greenbaum, P. McLean and E. Reid. *Nature (London)* 201:1131-1132, 1964.

As early as the first 4 wk. of feeding of 0.075% of carcinogens in the diet (either 4-dimethylamino-3-methylazobenzene (Me-DAB) or 4-dimethylamino-4'-fluorazobenzene (F-DAB) for 14-30 days) the liver NADP and NADPH₂ conc. fell below 60% of the control level ($224 \pm 18 \mu\text{g/g}$). With hepatomas produced after several mo. treatment with the azo dyes, this value diminished to 5% of control. In both cases, NADPH₂ accounts for most of the decline. F-DAB appears more active than MeDAB. The enzyme NAD-kinase was located entirely in the supernatant fraction of liver homogenates. Its only activity change was with the hepatomas where it decreased to 50% of control values. In the precancerous and tumorous livers there was no close correlation between NAD-kinase activity and the level of NADP and NADPH₂: the conc. of the nucleotides falls before there is any change in enzyme activity. The quotient of NADPH₂/NADP (exclusive of the acid-labile form of NADP) remains at control levels (3) in the precancerous state which in no way predicts the great drop (2) occurring in the hepatomas.

4-267 DOSAGE--RESPONSE CURVES FOR THE TERATOGENIC ACTIVITY OF TRYPAN BLUE. (E.) Beck, F. (Dept. Anat. Biochem., University Coll. S. Wales Monmouthshire, Cardiff, England) and J. B. Lloyd. *Nature (London)* 201:1136-1137, 1964.

Groups of 6-14 inbred Wistar rats were inj. s.c. with 5, 12.5, 25, 37.5, 50, 75, 100 or 200 mg/kg of trypan blue (free acid form) at 8.5 days of gestation; controls received 5 ml/kg of isotonic saline. Upon sacrifice at 20.5 days, external malformations and fetal resorption sites were noted. The number of implantations was unaltered by increase in dosage, whereas the dose-response curves for both resorptions and abnormalities increased until the optimum teratogenic dose (50 mg/kg) was reached. Beyond this dose the resorption rate increased at the expense of the abnormal as well as normal fetuses. Within the "teratogenic dose range" (5-100 mg/kg) any dose was capable of producing malformed offspring; however, no threshold below which the dye was inactive was demonstrated in this experiment.

64-268 BACTERIOSTATIC CHEMOTHERAPEUTIC AGENTS AND THE GROWTH OF MALIGNANT TUMOR. (E.) Uemura, R. (Dept. Surg., Hiroshima U. Sch. Med., Japan). *J. Int. Coll. Surg.* 41(3) (Pt. 1): 265-274, 1964.

After a review of the literature (43 references) on stimulation or inhibition of malignant tumor growth following the admin. of bacteriostatic agents, the author presents data on 97 pts. with malignant tumors who showed evidence of stimulation of malignant growth. In over 1,000 pts. treated with chloramphenicol (CP; total dose 11 g), isonicotinic acid hydrazide (INH; 7.8-39 g), PAS (350-9,400 g), penicillin (P; 3,000,000 U) or streptomycin (SM; 15-268 g), no evidence of inhibition of tumor growth was found. Laboratory investigation of blood catalase and cholinesterase activity, liver acid and alkaline phosphatase and catalase activity, mucoprotein volume, etc., were also conducted using the above agents + oleandomycin (OL), pyrrolidinomethyl tetracycline, pyrazinamide (PY) and tetracycline (T). The growth promoting effect of the above agents in animals bearing transplanted (1) azo dye-induced hepatoma, (2) Ehrlich carcinoma or Yoshida sarcoma, (3) methylcholanthrene-induced sarcoma and (4) nitrogen mustard-induced adenoma or leukemia was, resp.: +, +, + and 0, for INH; 0, +, +, and 0 for both kanamycin and OL; 0, 0, + and + for PAS; 0, +, 0 and 0 for both P and PY; +, +, + and + for SM; 0, +, + and 0 for T; +, +, + and 0 for combined INH, PAS and SM.

See also abstract nos.: 164, 169, 170, 173, 175, 176, 181, 182, 183, 187, 198, 205

VIRAL CARCINOGENESIS

- 64-269 MORPHOLOGY OF AN AGENT ASSOCIATED WITH A MURINE LEUKEMIA. (E.) Rich, M. A. (Lab. Cancer Res., Albert Einstein Med. Ctr., Philadelphia, Pa.) and L. W. Johns, Jr. Virology (New York) 20(2):373-376, 1963.

Swiss-ICR mice were given intrasplenic inj. of 0.2 ml of an extract, containing 500 µg/ml RNA, 300 µg/ml DNA and 220 µg/ml protein, prepared from spleens of Friend virus-infected mice. After 7 mo., 3/10 mice developed enlarged spleens and lymph nodes. Peripheral blood examinations revealed anemia, thrombocytopenia and a moderate leukocytosis with a prevailing atypical lymphocyte. Electron microscope studies of spleen and thymus sections disclosed 80-90 mµ particles with double limiting membranes characteristic of Friend virus and other murine leukemias. Blood concentrate studies also showed murine leukemia-associated particles (65-85 mµ), but with "tail-like" projections 22 mµ in diameter and varying from 85-210 mµ in length. Bacteriophage could not be demonstrated in the blood of these leukemic animals. Nonleukemic animals (controls) showed no such particles. These "tail-like" particles may represent a relatively mature stage of viral development. (See also CRA 1(6):#1119, 1963.)

- 64-270 THIN-SECTION ELECTRON MICROSCOPY OF THE MATURE LUCKE FROG KIDNEY TUMOR VIRUS. (E.) Lunger, P. D. (Rockefeller Inst., New York). Virology 22(2):285-286, 1964.

Mature viruses in the lumen of the proximal convoluted tube of the Lucke renal adenocarcinoma were observed with the electron microscope. The virus (diameter = 144 mµ) was shown to be enclosed by a thin membrane. Its nucleoid (diameter 55-77 mµ) was surrounded by a finely granular, continuous, partially defined shell of a thickness of 33 mµ with moderate electron density. Characteristic crescent-shaped accumulations of material similar to the shell in density and structure were present between the shell and inner surface of the membrane. The shell was a homogeneous layer with uranyl acetate. The virus showed significant differences from herpes virus.

- 64-271 AN ELECTRON MICROSCOPIC STUDY ON THE PARTICLES RESEMBLING THE MAMMARY TUMOR VIRUS IN ACINI AND HYPERPLASTIC NODULES IN MAMMARY GLANDS OF MICE. (E.) Miyawaki, H. (Dept. Path., Mie Prefectural U. Sch. Med., Japan) and Y. Nishizuka. Gann (Jap. J. Cancer Res.) 54(4):391-400, 1963.

When acini and hyperplastic alveolar nodules, which were present in the same mammary gland of female C3H/HeMs and (A/Jax x AKR)F₁ hybrid mice carrying the mammary tumor agent, were removed and subjected to electron microscopy studies and staining with trypan blue, both types of

tissues always showed the presence of virus-like particles identical in ultrastructure and mode of proliferation with those frequently found in mammary tumors (types A and B). Type A particles were vesicular, 70 mµ in diameter, and were found in the cytoplasm. Type B particles were round or oval, 100 mµ in diameter, had an electron dense, double outer membrane and were located predominantly inside the luminal and vacuolar spaces. At different stages of development, normal mammary gland tissue could not be distinguished from the hyperplastic nodules on the basis of the presence of virus-like particles. Ultrastructure comparison of acini, hyperplastic alveolar nodules, lactating glands and mammary tumors revealed no appreciable difference in submicroscopic morphology.

- 64-272 INTRANUCLEAR INCLUSION BODIES IN GLIOMA CELLS GROWN IN VITRO. (E.) Froelich, J. S., L. W. Lapham and V. R. Mumaw. J. Neuropath. Exp. Neurol. 23(1):197-199, 1964.

Cultures from a small percentage of 70 gliomas of different types were found to contain intranuclear inclusion bodies in considerable frequency. Of the 2 morphological types, Type I is variable in shape, bound by a nuclear membrane and filled with material indistinguishable from the cytoplasm. Nuclei containing these bodies are often of bizarre configuration. The inclusion bodies appear to be pools of enclosed cytoplasm. Type II inclusions are spherical or ellipsoidal in shape, have a prominent boundary often rimmed by clumps of chromatin and may or may not appear to contain varying amounts of eosinophilic material. Hypertrophic nucleoli with conspicuous eosinophilic granules occur in association with these inclusions. Electron microscopy showed virus-like particles in glioblastoma cells which developed Type II inclusions *in vitro*. Type II inclusion was also seen in giant cell carcinomas of the lung, giant cell melanomas and a few cases of anaplastic breast carcinomas. In the electron micrographs, the size of the particles was about 100 mµ.

- 64-273 DO CARCINOMATOUS NEUROPATHIES GIVE SUPPORT TO A VIRAL ORIGIN OF CANCER? (It.) Russell, D. (Bernhard Baron Inst. Path., London Hosp.). Gazz. Sanit. 34(12):669-670, 1963.

After a brief description of neurological disorders frequently disclosed by the necroscopic examination of cancer pts., including neuronal degeneration of the posterior root, partial inflammation of the brain and spinal cord and diffuse atrophy of the cerebellum, the author concludes that these pictures can be interpreted either as virus-induced disorders or as secondary effects of tumor toxic metabolites or as the result of interaction between tumoral antigens and antibodies.

64-274 VIRUS PARTICLES IN CULTURED LYMPHOBlasts FROM BURKITT'S LYMPHOMA. (E.) Epstein, M. A. (Middlesex Hosp. Sch. Med., London, W.1), B. G. Achong and Y. M. Barr. *Lancet* 1:702-703, 1964.

Electron microscope examination of cultured lymphoblasts from Burkitt's lymphoma revealed the presence of virus particles similar in appearance to herpes simplex virus, but whose diameters were 20% smaller (110-115 m μ). Immature particles with or without a nucleoid were observed in both the nucleus and cytoplasm; the mature agent was found only in the cytoplasm, within an enclosing cellular membrane, and was never seen outside the cells. Some of the infected cells also contained unusual bizarre cytoplasmic crystals with hollow tubular construction; these may be connected with the synthesis of viral protein units.

64-275 RESISTANCE OF CELLS CULTURED FROM TYPE 12 ADENOVIRUS-INDUCED TUMORS TO HETEROTYPIC ADENOVIRUS. (E., Abstract) Strohl, J. A. (Dept. Microbiol., St. Louis U., Mo.), J. C. Rouse and R. W. Schlesinger. *Bact. Proc.* 1964:132.

Both type 2 and type 12 adenovirus (assayed by a slightly modified plaque method) adsorbed equally well on 4 HT cell lines from hamster tumors (90% in 2-3 hr.), but normal hamster cell cultures (NH) adsorbed type 2 virus more slowly (90% in 4 hr.), while adsorption of type 12 was not measurable. The latter failed to multiply in either cell type. Type 2 virus yielded approx. 10³ PFU/cell in NH cells, but only 3/4 HT lines gave yields (<1 PFU/cell). In HT cultures infected with 10-100 PFU/cell, about 1% of the nuclei showed typical cytopathic changes, while the growth rate of such cultures was unchanged. The low yield of type 2 virus from HT cultures seems to be due to a few susceptible cells in populations of resistant cells.

64-276 IMMUNOFLUORESCENT AND HISTOCHEMICAL STUDY OF YABA TUMOR VIRUS REPLICATION IN CELL CULTURE. (E., Abstract) Yohn, D. S. (Roswell Park Mem. Inst., Buffalo, N.Y.), J. T. Race, Jr. and V. A. Haendiges. *Bact. Proc.* 1964:132.

The development of microscopically visible focal lesions produced by Yaba virus replication in a Cercopithecus kidney cell line, BSC-1, was followed daily for 14 days after infection by immunofluorescent and histochemical staining. Viral antigen synthesis first appeared in 48-72 hr. at paranuclear sites. These sites coalesced and formed a DNA-containing cytoplasmic inclusion body by the fifth day, with inclusions attaining maximal size within 8-10 days. The cytoplasm, hereafter, contracted and the inclusions were layered with RNA-containing material, rendering

it eosinophilic. Viral synthesis on the sixth day and inclusions on the tenth day were apparent in cells contiguous to those initially infected. (See also CRA 1(2):#268; *ibid.*, (3):#484, 1963.)

64-277 INDUCTION OF LEUKEMOID DISEASE IN MICE BY VIRUS-LIKE AGENTS DERIVED FROM CHILDREN WITH LEUKEMIA. (E., Abstract) Murphy, W. H. (Dept. Microbiol., U. Michigan, Ann Arbor), D. Furtado and E. Plata. *Bact. Proc.* 1964:133.

Virus-like agents were isolated from bone marrow specimens from children with leukemia after passage from 4-10x in human amnion, HeLa-S3, HeLa-Gey and Chang liver cells. These agents resembled the fowl leukosis viruses in size and structure, were filterable, resistant to inactivation at pH 3 or 56°C, did not possess adenovirus CF antigens, were chloroform sensitive, did not exhibit hemagglutinating or hemadsorptive activity, attained on passage a titer of 10⁶-10⁸/ml, exhibited auto-interference, were partially inhibited by FUDR (no details) in some cell lines, but failed to induce disease in newborn or adult inbred BALB mice up to 1 mo. after inoc. About 6-15 wk. after inoc., the mice exhibited gross pathological changes, 40,000-180,000 peripheral leukocytes/mm³, a mortality of approx. 50%, but no confirmation of leukemia upon histologic examination of tissues. Mice inoc. with control materials remained normal.

64-278 STUDIES WITH THE RAUSCHER MURINE LEUKEMIA VIRUS IN RANDOM-BRED SWISS MICE. (E., Abstract) Pienta, R. J. (Inst. Microbiol., Rutgers State U., New Brunswick, N.J.) and V. Groupe. *Bact. Proc.* 1964:133.

Random-bred Swiss mice from 6 sources were equally susceptible to infection with Rauscher leukemia virus. Mice from one source showed more resistance (longer latent period and less erythrocytopoiesis). Virus appeared in the blood and spleen of Swiss mice as early as 2 days after infection, reaching max. viral titers in 6-7 days and persisting as long as 95 days in the survivors. The peripheral blood of the infected mice showed that a true leukemia occurred. RBC did not exceed those of control mice. Erythropoiesis was confined to the spleen and liver. Hematocrit decreased significantly as the leukemia progressed. Mice passively immunized with potent antiserum gave rise to solid tumors, but no leukemia, and the tumors were transplanted for at least 8 passages. Attempts are in progress to isolate a virus from these tumors.

64-279 STUDIES ON A NEW MURINE LEUKEMIA VIRUS. (E., Abstract) Rich, M. A. (Lab. Cancer Res., Albert Einstein Med. Ctr., Philadelphia, Pa.), P. Meyers and J. Geldner. *Bact. Proc.* 1964:133.

Characteristics of this new murine leukemia virus

include: stability at -72°C , at 0°C for at least 3 days and at 37°C for 1 hr. but not for 6 hr.; sensitivity to ether and formalin; resistance to lyophilization. Cell-free homogenates of infected spleen, lymph node or thymus yield $10-10^7$ infectious U/ml. Sensitive to the virus are Swiss, Balb/C, and C3H mice and inbred rats; inoc. newborn rabbits, guinea pigs and hamsters show no disease to date. The virus can be propagated from infected cell cultures in normal mouse embryo cell cultures without CPE and passaged by cell transplant to immunologically suited mice; virus inoc. specifically protected mice against transplanted cells of the leukemia induced by that virus. Differences between this agent and other murine leukemia viruses were demonstrated by the use of specific neutralizing antisera. The latent period was proportional to the age at inoc., although leukemia was observed in mice inoc. as late as 6 mo.

- 64-280 IMMUNOGENIC VALUE OF MOUSE LEUKEMIA VIRUS INACTIVATED BY ILLUMINATED METHYLENE BLUE. (E., Abstract) Sinkovics, J. G. (Dept. Med., U. Texas M. D. Anderson Hosp., Houston), C. D. Howe, B. A. Bertin and C. B. Bordelon. *Bact. Proc.* 1964:133.

Although the Rauscher and Moloney mouse leukemia viruses were inactivated by a 10^{-5} dilution of illuminated methylene blue (exposure to visible light for 12-20 min. at 37°C), the virus retained fair antigenic potency, because the viral nucleic acids, but not the protein coat, were inactivated. Partially inactive Rauscher virus yielded weak antibody production and caused leukemia; the same virus, given with Freund's adjuvant, elicited better antibody production and no leukemia, although latent leukemia virus in the donor's spleen was proven by subsequent inoc. Therefore, antibody production and latent mouse leukemia virus may be compatible in the same host.

- 64-281 RELATIVE EFFICACY OF METHODS USED TO IMMUNIZE C58 MICE TO ISOGENIC TRANS-PLANTABLE LEUKEMIA. (E., Abstract) Murphy, W. H. (Dept. Microbiol., U. Michigan, Ann Arbor), C. Goll, N. Huber and L. Smith. *Bact. Proc.* 1964:133.

By repeated inoc. with high cell doses ($10^8/\text{ml}$), C58 mice could be immunized with either frozen or thawed, sonicated, or sonicated and lyophilized cell preparations, but these methods were no more effective than immunization with heated cells. Exposure to UV for 5 min. or more proved immunogenic, while an initial conc. of 10^7 line I_b cells exposed to a 1:500 dilution of formalin for 24 hr. at 4°C yielded a strongly immunogenic preparation, which was the most effective procedure. Mice thus immunized survived a challenge of 10^7 LD₁₀₀ of viable line I_b leukemia cells. Immunity persisted at least 10 wk.

- 64-282 ANALYSIS OF THE DEFECTIVENESS OF ROUS SARCOMA VIRUS. I. CHARACTERIZATION OF THE HELPER VIRUS. (E.) Hanafusa, H. (Virus Lab., U. California, Berkeley), T. Hanafusa and H. Rubin. *Virology* 22(4):591-601, 1964.

No significant differences were noted in heat inactivation rates at 37°C or in buoyant densities obtained by density gradient equilibrium technics in a high titer strain of Rous sarcoma virus (RSV) and Rous associated virus (RAV), its noncytopathic helper virus. Cross-absorption studies and virus neutralization tests showed that RSV did not possess any neutralizable antigens distinct from those present in RAV. Parallel growth curves were found for RSV and RAV. RAV preparations in high conc. induced interference to low doses of RSV even when the 2 viruses were added to the culture simultaneously and the interfering activity of RAV was sedimented with the infectious virus and neutralized by antiserum to RAV. This interference is due to the infectious RAV particle rather than to "interferon". RAV-infected cultures with a high degree of resistance to RSV were fully sensitive to infection with Western equine encephalomyelitis virus and vaccinia virus. (For earlier studies, see CRA 1(3):#506, 1963.)

- 64-283 DIFFERENTIAL RESPONSIVENESS OF ROUS SARCOMA VIRUS STOCKS TO SPECIFIC CELLULAR RESISTANCE INDUCED BY AVIAN LEUKOSIS VIRUSES. (E.) Hanafusa, T. (Virus Lab., U. California, Berkeley), H. Hanafusa and H. Rubin. *Virology* 22(4):643-645, 1964.

In a study of relative sensitivities to Rous sarcoma virus (RSV) #8 infection, preexisting infection with Rous associated virus (RAV) and resistance-inducing factor (RIF) in cultures from chick embryos termed "good resisters" resulted in a max. decrease in sensitivity of 1000 to 10,000-fold. The max. decrease was only tenfold in cultures from embryos termed "poor resisters". These characteristic levels of resistance remained constant in 10 successive transfers and seem to be genetically determined. High degrees of resistance were observed in both good and poor resister cultures when either RSV(RIF) or RSV(RAV) was used to challenge cultures infected with leukosis viruses, although more resistance was shown to challenge by RSV(RIF) than to challenge by RSV(RAV) by both good and poor resister cultures. No evidence for intermediate levels of resistance was seen and no infectious agent capable of interconverting the resister status of the 2 types of cultures was detected when the media between the cultures prior to infection with leukosis viruses were switched. (See also CRA 1(3):#506, 1963.)

- 64-284 STUDIES OF THE EARLY STAGES OF ROUS SARCOMA VIRUS INFECTION IN VITRO. (E.) Ting, R. C. (NCI, Bethesda). *Virology* 22(4):568-574, 1964.

results of chick embryo cell infection with a 3C1 strain (h^+) of Rous sarcoma virus (RSV) challenged at various time intervals with host-range mutant strain (h^d) of RSV indicate that the production of h^+ virus is about the same in all cases, whereas that of h^d virus decreased as the time interval between h^+ infection and challenge increased. The effect first became noticeable after a 4-hr. interval. In a mixed infection, the yield of h^+ virus was suppressed as the h^d virus to a certain extent. The growth curve of chick or duck embryo cells infected at low multiplicity differs from that of established virus cells by showing a 1 or 2 division delay before starting to grow exponentially. The growth of h^d -infected chick or duck cells corresponded well with the latent period of the virus.

4-285 NUMBER OF GENES CONTROLLING RESPONSE OF CHICK EMBRYO CHORIOALLANTOIC MEMBRANES TO TUMOR INDUCTION BY ROUS SARCOMA VIRUS. (E., Abstract) Bower, R. K. (Grad. Res. Inst. Baylor U., Dallas, Tex.). Bact. Proc. 1964:134.

In a study to determine the number of pairs of genes in chick embryos controlling the response of the chorioallantoic membranes (CAM) to tumor induction by Rous sarcoma virus (RSV), CAM from White Leghorn, Giant Jungle Fowl, F₁ generation crossbred and F₂ generation crossbred chick embryos were inoc. with RSV and examined 8 days later for tumor induction. Statistical analyses, which included only CAM on which precise tumor counts were made and CAM with estimated tumor counts, yielded estimates of 1.05 pairs of genes from CAM with precise tumor counts and 1.02 pairs of genes from CAM including all tumor counts. It was concluded from the data that only one pair of genes was involved. It appeared that the penetrance of these alleles was incomplete, and there was evidence that susceptibility was partially dominant to resistance.

4-286 TITRATION OF ROUS SARCOMA VIRUS ON THE CHICK EMBRYO CHORIOALLANTOIC MEMBRANE. (E., Abstract) Vrba, M. (Inst. Exptl. Biol. Genet., Czechoslovak Acad. Sci., Prague). Acta Virol. 6:525-533, 1963.

The chorioallantoic membranes (CAM) of non-inbred White Leghorn chick embryos were inoc. on day 9 of incub. with Rous sarcoma virus (RSV; diluted to 10^{-3} , $10^{-3.3}$, $10^{-3.7}$, 10^{-4} ; inj. of 0.1 ml) and the morphological and quantitative responses were read on day 18 or 19 of incub. 50 embryos inoc. with RSV (day 12 at 10^{-3} dilution), 34 contained malignant centers (MC) which, however, did not correspond to Poisson's distribution and had the character of left-sided asymmetrical distribution. The percentage of resistant embryos (i.e. whose CAM was unaffected by RSV) in breeds A, B, C, and D of White Leghorn chicks was 28%, 58%, 62%, and 72%, resp.; when breed A embryos alone were used in 5 different

experiments, the percentage of resistant embryos was 28%, 31%, 34%, 37%, and 35%. When day 12 and day 9 embryos were inoc. with the same dilution of RSV and observed on day 19 and 18, resp., MC formation was quantitatively higher for day 12 CAM. The number of MC formations showed an approx. linear relationship to the RSV dilution, although with large av. dispersion. The neutralizing capacity of some duck sera was studied and the author noted that the sera from ducks resistant to RSV infection and the sera from ducks sensitized to RSV infection cannot be regarded as sera possessing a neutralizing effect against RSV. 6-Azauridine (AZUR) reduced the effect of RSV on the CAM by approx. 50% if AZUR was admin. to the CAM together with the virus suspension.

64-287 LEUKEMIA IN GERM-FREE MICE. (E., Abstract) Pollard, M. (Lobund Lab., U. Notre Dame, Ind.). Bact. Proc. 1964:134.

Lymphatic leukemia (etiology not yet determined) was induced in GF C3H mice by X-rays. After i.p. inoc. of 2-day-old GF C3H mice with 0.1 ml filtrate of Gross strain A leukemia virus, examination of 19/25 surviving mice showed that they were symptom- and lesion-free for 9 wk. after inoc. They then became rough, dyspneic and their first lesion was an enlarged thymus with numerous mitotic lymphoid cells. Progressively increasing reaction zones were noted in the lymph nodes. Thymus, lymph nodes, and visceral organs were swollen, and normal structures became obscured by the leukemic cells. The presence of occult radiogenic leukemia and the absence of a bacterial flora did not alter the susceptibility to this leukemogenic virus. The leukemic lesion appears to evolve from hyperactivity of reaction zones in lymph nodes, subsequent to thymus hyperactivity.

64-288 EFFECT OF STRESS ON SUSCEPTIBILITY OF MICE TO POLYOMA VIRUS INFECTION. (E., Abstract) Chang, S.-S. (Dept. Med., U. California, Los Angeles) and A. F. Rasmussen, Jr. Bact. Proc. 1964:134.

Polyoma virus susceptible (AKR), resistant (C57Bl) and intermediately susceptible (F₁ C57Bl x AKR and W-BRVS) mice were inoc. with polyoma virus and subjected to high intensity sound stress 3 hr./day x 6, followed by avoidance learning stress, 6 hr./day for 2 wk. This stress produced an increased incidence of tumors in all strains with the tumor incidence decreasing in the following order: AKR, (C57Bl x AKR)F₁, W-BRVS, and C57Bl. When the mice were subjected to avoidance learning stress only, starting from day 7 postinfection, there was no significant difference in tumor incidence. (See also 1(1):#102, 1963.)

64-289 MICROKINEMATOGRAPHIC STUDY OF THE CYTOPATHOGENIC EFFECT OF A VACUOLIZING VIRUS (SV 40) ON THE RENAL CELLS OF CERCOPITHECUS

AETHIOPS. (Fr.) Pruniéras, M. (Dept. Hygiene, U. Lyon Sch. Med., France), Y. Chardonnet and R. Sohier. Ann. Inst. Pasteur (Paris) 106(1): 1-17, 1964.

A microcinematographic study of cultures of African green monkey kidney cells infected with SV40 virus confirmed previous reports that intranuclear viral inclusions were followed by cytoplasmic vacuolization. In addition, the behavior of other cells suggested that viral material may also be re-transferred from the nucleus to the cytoplasm, by means of small cytoplasmic vacuoles which clustered about the nucleus in large numbers and then penetrated spontaneously appearing areas of deep invagination in the nuclear membrane, which either disappeared or became extremely thin at the point of deepest penetration. In some cases, these vacuoles and an extension arising from the nucleolus came into contact or close approximation, which was maintained for several min. prior to the sudden retreat of the vacuoles to the cytoplasm, where they clustered again around a nucleus which had resumed its original shape. Nucleoli were also seen to undergo early hypertrophy after SV40 infection, followed by the casting off of some dense material appearing for the first time at the periphery of the nucleolus. This material, identified tentatively as newly-formed chromatin blocks, then migrated through the nucleoplasm and crossed the nuclear membrane. Following expulsion of this material from the nucleus, no mitoses were noted during 23 days of observation after inoc. and the cells died without having shown the cytoplasmic vacuolization previously reported as a part of the cytopathogenic effect of SV40. The authors suggest that this effect of SV40 on the nucleolus may be related to the ability of the virus to transform cells in tissue cultures.

64-290 CYTOLOGICAL AND CYTOCHEMICAL STUDIES OF PRIMARY AND TRANSPLANTED KIDNEY CULTURES OF AFRICAN GRIVET MONKEYS (CERCOPITHECUS AETHIOPS) INFECTED WITH SV40. (Rus.) Karmysheva, V. Ia. (Inst. Poliomyel. Encephal., Acad. Med. Sci. USSR, Moscow), N. M. Shestomalova, V. N. Reingol'd, G. I. Koliaskina and M. P. Chumakov. Vop. Virus. 8(4):460-465, 1963.

Incubation for 48 hr. of SV40 (strain A-426) with primary and transplanted BS=C1 cells of the grivet kidney led to the same cytopathologic changes in both cultures. As the result of infection the first changes occurred in the nuclei; they became swollen and increased in size more than 200%. The nucleoli became deformed and often gave a positive Feulgen reaction (oxyphilic, DNA-containing inclusions). Vacuoles were formed in the cytoplasm of a number of cells. Glycogen content was decreased, particularly around the vacuoles, while lipid was increased. Mitotic activity was not changed during the first 2 days after infection but after that there was an increase in cells with irregular mitotic figures.

64-291 VIROLOGICAL AND SEROLOGICAL DATA ON LATENT SV40 INFECTION IN THE RHESUS MONKEY (MACACA). (Rus.) Koliaskina, G. I. (Inst. Poliomyel. Encephal., Acad. Med. Sci. USSR, Moscow). Vop. Virus. 8(4):450-453, 1963.

During a 42-day period of observation, 15 intact, control grivet monkeys did not show any spontaneous vacuolization of their kidney cells. When 100 primary rhesus kidney cell cultures and decantates were examined after 7, 14 and 21 days, SV40 was found in 29, 37 and 47 cultures, resp. SV40 antibodies were detected in 26/74 rhesus serum samples studied; in 3 of the negative cases SV40 was detected whereas in the case of 1 positive serum, no SV40 was found in the decantate.

64-292 PRESENCE OF ANTIBODIES TO MONKEY VIRUS SV40 IN HUMAN SERUM. SEROLOGICAL PROOF OF INFECTION FROM MONKEYS AND KIDNEY CULTURES. (Rus.) Chumakova, M. Ia. (Inst. Poliomyel. Encephal., Acad. Med. Sci. USSR, Moscow), M. P. Chumakov, L. B. El'bert, G. I. Avgustinovich, N. M. Ral'f, M. K. Voroshilova, G. P. Taranova and V. O. Tapupere. Vop. Virus. 8(4):457-459, 1963.

Specific antibodies to SV40 were found in 30-86% of persons having contact with rhesus monkeys or their kidney cultures. Equally, the antibodies were also found in 50% of children who were inoc. 3x with Salk vaccine prepared with rhesus kidney tissue. No antibodies were formed in persons receiving 1-2 inj. of Salk vaccine and 3-6 p.o. doses of Sabin vaccine. It is suggested that the conc. of virus which could be contained in one dose of vaccine admin. p.o. is insufficient to cause the infection.

64-293 ELECTRON MICROSCOPY OF VACUOLIZING VIRUS SV40 IN THE CELLS OF AFRICAN GRIVET MONKEY KIDNEY CULTURES AND IN VIRAL SUSPENSIONS. (Rus.) Shestomalova, N. M. (Inst. Poliomyel. Encephal., Acad. Med. Sci., USSR, Moscow), V. N. Reingol'd, G. I. Koliaskina and M. P. Chumakov. Vop. Virus. 8(4):466-470, 1963.

The infection of kidney cells by SV40 (strain A-426) takes place in the nucleus, and the ability to infect is attributed to viral DNA and host RNA. The content of the latter was increased in the nucleolus; there was also increase in ribonucleoprotein in cytoplasm that had become vacuolated. The mitochondria underwent structural change and organoids degenerated while the chromatin underwent rearrangement. The nucleus increased in size and later viral particles were noted. In the nucleolus a spongy substance was noted which contained coarsely granular particles. Spherical viral particles were seen in the nucleus and cytoplasm which were 33 and 38 m μ in diameter, resp. In cells with massive accumulations of viral particles, the particles were tubular in form and were 30 m μ in diameter when sectioned. In viral suspensions treated by the negative

aining technic, the particles were spherical and measured 45 mμ in diameter; both spherical and filamentous viral forms were detected by this technic.

- 294 THE USE OF THE FLUORESCENT ANTIBODY TECHNIC FOR THE LOCALIZATION OF SV40 THE CELL AND ITS RAPID DETECTION IN VACCINE. (Rus.) Dzagurov, S. G. (Inst. Poliomyel. Encephal., Acad. Med. Sci. USSR, Moscow), M. P. Chumakov, V. Ia. Karmysheva, G. I. Koliaskina, A. A. Graevskaia, N. P. Kurochkina and L. B. Nosian. Vop. Virus. 8(4):471-475, 1963.

The fluorescence of grivet monkey trypsinized kidney tissue infected with SV40 (strain A-426) up to 10-12 dilutions, and subsequently treated with immune rabbit globulins conjugated with fluorescein isothiocyanide, was first evident after 18 hr. First the fluorescence of nuclei was observed, but toward 120 hr. the cytoplasm was fluorescing even with minimal amounts of SV40. The fluorescence was specific for each stage of the infectious process and was absent when the cultures were treated for 30 min. with non-conjugated globulins. In similar studies of 45 live cultures of polio vaccine, grown on rhesus kidney, the presence of SV40 was established in 19/45 when the cytopathic method was used compared to 29/45 when the fluorescence method was employed. These studies show that the fluorescent antibody technic is more sensitive than the cytopathic method, however, further studies are necessary to confirm its specificity.

- 295 A CONTINUOUS CELL LINE FROM SV40-VIRUS-INDUCED TUMOR IN SYRIAN HAMSTER. (Rus.) Gavrilov, V. I. (Inst. Virol., Acad. Med. Sci. USSR, Moscow), N. N. Vasil'eva, N. N. Monova and R. G. Emieva. Vop. Virus. 8(5):556-559, 1963.

Continuous *in vitro* cultivation of explants from SV40 virus-induced tumor resulted in the development of a cell culture designated CA-SV40-63. Cytologically, it was characterized by cellular nuclear polymorphism, vacuolization of nuclei, normal mitosis, rearrangement of chromatin and formation of giant multinucleated cells and plasmas. It was 100% transplantable to 0.5-2-month-old Syrian hamsters (40,000-140,000 cells, i.p.); tumors developed after 8-12 days. CA-SV40-63 produces active SV40 and is sensitive to the following viruses: vaccinia, monkey pox B, Newcastle, poliomyelitis (types 1-2) and Coxsackie B₁; it was resistant to rhesus herpesviruses.

- 296 ANTIBODIES TO SV40 IN MONKEYS OF VARIOUS SPECIES. (Rus.) Chumakova, V. Ia. (Inst. Poliomyel. Encephal., Acad. Med. Sci. USSR, Moscow), G. I. Avgustinovich

and T. I. Zavodova. Vop. Virus. 8(4):452-456, 1963.

Sera of baboons, rhesus and grivet monkeys were incub. with SV40 (strain A-426; 100 "BOE") for 18-20 hr. It was found that, in rhesus, the complement fixation and neutralizing antibody reactions were positive in 96% and 98% of the samples, resp. Grivet monkey and baboons, when kept isolated, had no antibodies; incidence of positive results depended on the degree of contact with rhesus monkeys. On the whole, the titers of rhesus monkeys and baboons were higher than those of grivet monkeys, yet there was no correlation between the level of complement and antibodies.

- 64-297 LUMINESCENT MICROSCOPY STUDY OF POLYOMA VIRUS ANTIGEN IN TRANSFORMED CULTURES OF HAMSTER EMBRYO. (Rus.) Varbosanidze, E. Sh. (Inst. Oncol. Ministry Health Georgian SSR, Tbilisi) and I. S. Irlin. Vop. Virus. 8(5):556-559, 1963.

The presence of polyoma virus SE (strain 2510) antigen was established by the fluorescent technic in mouse and hamster infected embryonal tissue. In mouse tissue, 24-48 hr. after infection, many nuclei were fluorescent with marked increase after 72-96 hr. At this time the cytoplasm also exhibited some degree of fluorescence, and toward 120 hr. (peak of total cytopathic effect) the cells appeared as fluorescent spheres (controls showed no fluorescence). Hamster tissue gave the same results but it was not possible to determine the changes in the positions of the antigen as was possible in mouse tissue. The transformed, infected cultures, having lost the virus, had no antigen; when examined by Coon's indirect method no fluorescence could be observed.

- 64-298 ROUS VIRUS-INDUCED SARCOMA IN HAMSTERS (STRAIN KARR). (Rus.) Shevliagin, V. Ia. (N. F. Gamaleya Inst. Epidemiol. Microbiol., Acad. Med. Sci. USSR, Moscow). Vop. Virus. 8(5):617-619, 1963.

The growth of Rous virus sarcoma (s.c. inoc.) was evident after 4-5 wk. in newborn hamsters; in 2-week-old animals the incub. period was longer. In both groups it was indirectly proportional to the quantity of admin. material. Microscopically, the tumors could be divided into 2 different groups: one type was a moderately growing, small, solid fibroma, sometimes resembling fibrosarcoma; the other was rapidly growing, soft, with a necrotic center, often mixed with skin and ulcerated polymorphocellular sarcoma with a large number of giant cells. Both types always led to pulmonary metastases and death. The second tumor type was freely transplantable (s.c. or i.p.) to newborn and adult hamsters. It was not possible to isolate the virus from the animals or to produce passages with cell-free extracts.

- 64-299 SUBMICROSCOPIC STRUCTURES IN THE CELLS OF HAMSTER EMBRYONIC TISSUE TRANSFORMED BY POLYOMA VIRUS IN VITRO. (E.) Bykhovsky, A. F. (Dept. Immun. Oncol., Gamaleya Inst. Epidemiol. Microbiol., Moscow) and I. S. Irlin. Virology 22(3):434-436, 1964.

Three wk. after infection with polyoma virus of hamster embryonic tissue cultures, examination of 7 primary transformation foci revealed no viral particles but several tubular structures (Type A, B, C) localized in the cytoplasm of the transformed cells and not found in non-transformed hamster embryonic cells. At 6-8 wk. after infection, cultures consisted of completely transformed cells. After many passages (some for over a yr.), no traces of polyoma virus or virus antigen were found, but structures identical to Type C of the primary focus were present, and a looser tubular structure (Type D) was now apparent. In 6 normal clones from infected cultures possessing typical oriented monolayer growth identical to clones from noninfected cultures of hamster embryonic tissue, similar structures were not seen with the electron microscope.

- 64-300 EXPERIMENTAL STUDIES ON THE ONCOGENIC ACTION OF THE VACCINIA VIRUS. (Rum.) Ilie, B. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest). Stud. Cercet. Inframicrobiol. 14(5):625-634, 1963.

Three groups of H mice of both sexes were inoc. with Ehrlich ascites filtrate alone, filtrate + vaccinia virus, and vaccinia virus alone. Among the 37/150 survivors after 8 mo., incidence of malignancies/number of mice was, resp.: 1/14; 7/13 and 2/10. The tumor types found were hepatic, splenic and lymph node reticulum cell sarcomas, mammary adenocarcinomas, and multitemporal forms, showing that under certain conditions the vaccinia virus has definite carcinogenic activity. (See also CRA 1(9-10):#1753, 1964.)

- 64-301 ETIOLOGIC INVESTIGATIONS IN HODGKIN'S DISEASE. IV. CULTIVATION IN HUMAN EMBRYO CELLS OF VIRUS ADAPTED TO THE WHITE MOUSE. (Rum.) Cajal, N. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest), M. Cepleanu, Y. Sorodoc, V. Lotreanu and A. Schäcter. Stud. Cercet. Inframicrobiol. 14(5):577-581, 1963.

See CRA 1(11):#1952, 1964.

- 64-302 STUDIES ON THE ETIOLOGY OF MALIGNANT LYMPHOGRANULOMATOSIS (HODGKIN'S DISEASE). VI. ATTEMPTS AT LOCALIZATION OF INTRACELLULAR BIOSYNTHESIS OF THE VIRUS BY MEANS OF ACRIDINE ORANGE FLUORESCENT STAINING. (Rum.) Cajal, N. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest), M. Cepleanu, S. Mihail, V. Lotreanu and Y. Sorodoc. Stud. Cercet. Inframicrobiol. 14(6):691-695, 1963.

Human embryonal cell cultures infected with a virus isolated from pts. with Hodgkin's disease (see CRA 2(2):#301, 1964) showed upon staining with acridine orange DNA which was accumulated in the cytoplasm, thus indicating a biosynthetic role for the isolated agent. From the results of the experiment, the authors feel justified in the assumption that DNA is the only nucleic acid present.

- 64-303 STUDIES ON THE ETIOLOGY OF MALIGNANT LYMPHOGRANULOMATOSIS (HODGKIN'S DISEASE). V. PRIMARY SUSCEPTIBILITY OF 11 CELL STRAINS TO INFECTION BY VIRUS ADAPTED TO HUMAN EMBRYO CELLS. (Rum.) Cajal, N. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest), I. Aderca, M. Cepleanu, M. Iftimovici, Y. Sorodoc and V. Lotreanu. Stud. Cercet. Inframicrobiol. 14(6):685-690, 1963.

Two virus strains isolated from lymph nodes of Hodgkin's pts. and carried in chick embryos and later propagated in white mice, were tested on the following cell strains: human embryonal kidney, lung and chorion, mouse embryo, KB, ERK, HEp-2, AM, HeLa, SCH (Cynomolgus chord), HLS, and C. Time of appearance of cytopathic effects with giant cells (see CRA 2(2):#301, 1964) and their intensity were recorded. It was found that these effects closely approximate those produced by the Motol virus (isolated by Kubelka from cases of infectious hepatitis). However, the 2 strains can easily be differentiated from the Motol virus, for the latter grows only on HEp-2 and ES cell strains and on embryonal mouse cells, while the Hodgkin's virus grows equally well in all eleven cell lines.

- 64-304 DATA ON THE SUBMICROBIAL ETIOLOGY OF HUMAN CUTANEOUS RETICULUM SARCOMA. (Rum.) Cajal, N. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest), M. Cepleanu, N. I. Ionescu and S. Dumitrescu. Oncol. si Radiol. 1(3):225-228, 1962.

See CRA 1(6):#1144, 1963.

- 64-305 EXPERIMENTAL STUDIES ON THE VIRAL ETIOLOGY OF HUMAN AND MOUSE LEUKEMIA; ATTEMPTS AT TRANSMITTING THE DISEASE TO LABORATORY ANIMALS. (Rum.) Nastac, E. (Inst. Inframicrobiol., Bucharest), B. Anagnoste and G. Balmus. Oncol. si Radiol. 1(1):41-46, 1962.

See CRA 1(3):#513 and ibid., (4):#701, 1963.

- 64-306 CONSIDERATIONS ON TRANSFUSIONS WITH LEUKEMIC BLOOD IN NEWBORNS. (Por.) Assumpção Bicalho, S. (Dept. Med., U. Minas Gerais, Belo Horizonte, Brazil) and J. Guerra Lages. Hospital (Rio) 65(1):215-221, 1964.

Three mo. before diagnosis of chronic lymphatic

leukemia the blood from a 28-year-old pt. was given (in amounts of 40 to 100 ml) to 4 male infants (5-7 mo. of age) with severe gastrointestinal infection and dystrophy. Three died, 9, and 14 mo., resp., after the transfusion; autopsy revealed no leukemic lesions. The 4th child was alive at time of report; he was periodically examined every 4 mo. and presented severe anemia and dystrophy. His recovery was slow.

4-307 OCCURRENCE OF TUMORS, LEUKEMIAS, AND RENAL CHANGES IN MICE AFTER INOCULATION OF CELL-FREE TUMOR FILTRATES. (Ger.) Remayer, N. (Inst. Path., U. Freiburg/Br., Germany), H. Noltenius and A. Stockinger. *Naturwissenschaften* 51(5):116, 1964.

Cell-free filtrates prepared from a transplantable lymphosarcoma (LF) originally induced by ax fibers and from a transplantable ascitic mammary carcinoma (ZFTm) were inoc. into newborn mice according to a previously described technic. Among 56 random-bred PI mice treated with LF 24 hr. after birth, there were, after 3-23 mo., 12 mammary tumors, 7 leukemias, 6 other tumors (2 round cell sarcomas, 1 pulmonary alveolar cell carcinoma, 2 squamous cell epitheliomas, 1 mesenteric adenocarcinoma) and 1 parotid tumor. In 39 Agnes Bluhm (AB) mice treated with LF the yield was 9 leukemias, 2 parotid tumors, and 3 other tumors; among 28 AB mice inoc. with ZFTm 12 or 24 hr. after birth there were 8 leukemias, 1 mesenteric tumor, and 1 hemangioma of the urinary bladder. Kidney changes (nodular pigmentation of interstitial cells 4 wk. after inoc.) were seen in 87% of the PI and in 77% of the AB strain. It is assumed that the mammary and parotid tumors obtained were caused by a polyoma virus, which also may have induced the kidney changes, while the leukemias are attributed to a filterable leukemia virus.

4-308 HUMAN CANCERS AND VIRUS. (Fr.) Zagury, D. *C.R. Assn. Anat.* (120): 1364-1368, 1964.

Observed under the electron microscope were specimens of 3 gastric carcinomas and 1 adenocarcinoma of the pancreas head fixed immediately after their removal from the tumor during surgery. Among a number of preparations observed, virus was detected in only 3 instances. Virus-like particles were seen inside some cells in the cytoplasm or in the intracytoplasmic vacuoles in a geometric pattern but sometimes they were randomly arranged. The virus could also assume the aspect of "viroplasm", that is a diffuse mass 0.5-2 μ in diameter consisting of more or less parallel linear elements which were 7.0 $m\mu$ in thickness or of round granules and small vesicles 22 $m\mu$ in diameter in the center of which one could sometimes see a small grain. The affected cancerous cells presented signs of

degeneration with nuclear lysis and swelling of the mitochondria in contact with the virus-particles. No virus was detected in typical cancer cells.

64-309 MOUSE ERYTHROLEUKAEMIA OF VIRAL AETIOLOGY. (E.) Siegel, B. V. (Dept. Path., U. Oregon Sch. Med., Portland), W. J. Weaver and R. D. Koler. *Nature (London)* 201: 1042-1043, 1964.

Female 5-week-old BALB/c/jax mice inoc. with 0.2 ml of a 10% suspension of spleen containing Rauscher virus showed reticulocytosis, anemia, and an increase in nucleated cell count, reaching a max. at 6 wk. The proliferating cells were identified as erythrocytic in origin. By the 3rd wk., blood smears demonstrated progressive changes consisting of polychromatophilia, anisocytosis and Howell-Jolly bodies of mature erythrocytes and an increase in total nucleated cells. Intact cells were mainly identified as metarubricytes, rubricytes, and prorubricytes; the latter two (in blood smears and imprints of spleen and liver) showed increased parachromatin resembling that in pernicious anemia and di Guglielmo's disease in man. Of 135 mice, 56 were killed experimentally over 8 wk.; 77 died 5-8 wk. post-inoc.; two 9-wk. survivors showed gross evidence of marked hepatosplenomegaly. No lymphocytic or monocytic proliferation was seen. The development of lymphocytic leukemia subsequent to the induction of an erythroleukemic syndrome is under investigation. (See also CRA 1(4):#728, 1963.)

64-310 PAS-POSITIVE GIANT CELL IN THE CORTEX OF THE THYMUS IN HIGH INCIDENCE AND LOW INCIDENCE LEUKEMIA MOUSE STRAINS. (Jap., Abstract) Ishidate, M. (Sasaki Res. Inst., Japan) and D. Metcalf. *Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.)* 52:221-222, 1963.

A comparative histological study of the cortex of the thymus with specific reference to PAS-positive giant cells was performed in mice with high incidence of leukemia (AKR, (AKR x C3H)F₁), and in those with low incidence (C3H, (AKR x C57BL)F₁). The mitotic index of lymphocytes in the cortex was studied in the PAS area (the area with PAS-positive cells surrounded by lymphocytes) and in the non-PAS area (the area without PAS-positive cells). The index was extremely high in the PAS area of AKR mice and was >3x that of the non-PAS area. However, no significant difference between the two areas was found in C3H mice. The thymus became atrophic after admin. of cortisone (0.2-1.0 mg x 1) but PAS-positive cells showed resistance against cortisone and increased in number. This effect was noted in both C3H and AKR mice. The authors believe that PAS-positive cells play an important role in the proliferation or regeneration of lymphocytes in the thymus.

- 64-311 FRIEND VIRUS INDUCED ASCITIC TUMOR. (Jap., Abstract) Ohoshi, S. (Dept. Path., Nat. Cancer Inst., Japan), T. Aoki, R. Sato and T. Baba. Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.) 52:238-239, 1963.

The liver and spleen from ddOM strain mice 9-10 wk. after infection with Friend virus, when inoc. into the same strain, induced s.c. tumors. This tumor mass, removed from a mouse in generation 17, when transplanted i.p. in ddOM and ddY mice induced ascitic type tumors (100% and 77% takes, resp.). When inoc. into other strains, this tumor induced ascitic type tumors in 80% ddN, 21% SMA and 0% C3H/He. While the Friend virus caused ascitic tumors, no virus was found in the tumor cells.

- 64-312 ROLE OF THE THYMUS AND VIRUS IN LEUKEMOGENESIS IN MICE. IV. LEUKEMOGENIC EFFECTS OF TRANSPLANTED THYMUS IN MICE. PRELIMINARY REPORT. (Jap., Abstract) Nakakuki, K. (Dept. Path., Mie U., Japan) and Y. Nishizuka. Nippon Ketsueki Gakkai Zasshi (Acta Hemat. Jap.) 26(3,4):388, 1963.

Thymic grafts from AKR male mice of the same age were transplanted (s.c.) into 26-40-day-old (A/Jax x AKR)F1 females (45). When observed to age 24 mo., 12/45 (26.7%) developed nonthymic leukemia while only 2/30 (6.7%) developed leukemia in untreated controls. 20-Methylcholanthrene (MC; 60 µg, s.c. x 1) was inj. into Swiss mice of 3 ages: 24-hr., 10-day, and 30-day. Incidence of leukemia within 12 mo. after delivery was, resp.: 2/30, 4/25 and 4/16. When 40-day-old male Swiss mice which had previously been thymectomized received a thymus graft from the same aged mouse treated with MC (60 µg), leukemia developed in 4/7 (57%). No leukemia developed in 10 thymectomized controls.

- 64-313 RESISTANCE AGAINST ISOTRANSPLANTATION OF MOUSE TUMORS INDUCED BY ROUS SARCOMA VIRUS. (E.) Sjögren, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden) and N. Jonsson. Exp. Cell Res. 32(3):618-621, 1963.

Tumors were obtained in newborn mice of the strains A/Sn, A.BY, A.CA and C57BL/KL after s.c. inoc. of the Schmidt-Ruppin strain of Rous sarcoma virus. Homografts were made of tumors from passages 3-12 for each of the strains. Some mice were given homograft pretreatment with tumors of non-Rous origin. Adult recipients were challenged with genetically compatible tumor cells. Isotransplantation resistance was demonstrated by mice who received Rous tumor homografts prior to the test challenge, while homografts with non-Rous tumors induced no resistance. The Rous tumor homograft-induced resistance was not abolished by 400 r X-rays 24 hr. prior to the test challenge. A weak resistance was induced by Rous virus in the form of Rous chicken tumor homogenate. This

demonstrated that tumors induced by homografts of other Rous tumors and those induced by Rous virus possessed common antigen(s).

- 64-314 BIOASSAY OF FOWL LEUKOSIS VIRUS IN CHICKENS BY THE INOCULATION OF 11-DAY-OLD EMBRYOS. (E.) Piraino, F. (Virus Lab., City Milwaukee Health Dept., Wisc.), W. Okazaki, B. R. Burmester and T. N. Fredrickson. Virology 21(3):396-401, 1963.

Comparative assays of leukosis strains RPL 12, RPL 25, RPL 26, and RPL 29 were conducted by i.v. inoc. of 11-day-old embryos and 14-day-old chickens of the inbred White Leghorn 151 line with 5% filtered extracts of liver from leukosis-strain induced erythroblastotic chickens. After inoc. embryos were held for 46 days, chickens for 77 days. Erythroblastosis was the primary specific neoplasm induced, but some embryos also developed fibrosarcomas, endotheliomas, nephromas, chondromas and hemorrhages. Equivalent quantal responses in terms of probits were higher in embryo inoc. than in chick inoc. by 2.0 log₁₀ dilution for 3 strains and 0.7 log₁₀ dilution for 1 strain. A lower level of virus conc. is needed to induce erythroblastosis in inoc. embryos than in inoc. chicks.

- 64-315 EXPERIMENTAL INVESTIGATIONS IN HUMAN LEUKEMIA. III. EFFECT OF THE PATHOLOGIC PRODUCTS OF HUMAN LEUKEMIA ON THE DEVELOPMENT OF CHICK EMBRYO. (Rum.) Nastac, E. (Inst. Infra-microbiol., Acad. Sci. Rumania, Bucharest), G. Popescu, G. Balmus, G. Rutter, G. Isaia, M. Lungu and V. Anagnoste. Stud. Cercet. Infra-microbiol. 14(6):713-723, 1963.

Blood, or serum from a pt. with acute myeloid leukemia (not subjected to any treatment) was serially inoc. into the yolk sac or chorioallantoic membrane of 6-8-day-old chick embryos. Three to 8 days after inoc., 44-69% of the embryos died (starting from the 10th-11th passage) while of those which hatched, 25% showed congenital malformations (coxofemoral luxations, adductions (30-50%), torsion of the legs (70-90%), and dystrophy). One of the chicks showed leukemia (WBC = 150,000) and marked erythroblastosis. Histologic examinations revealed infiltrative and proliferative changes, both of the embryonic tissues and membranes; these effects continued to be seen after serial inoc. The lesions were more pronounced when the material was inoc. into the egg yolk. It is concluded that a pathogenic agent has been isolated from the blood and serum of a pt. with acute myeloid leukemia.

- 64-316 EXPERIMENTAL INFECTION AND HISTOPATHOLOGICAL AND HISTOCHEMICAL STUDIES OF A HUMAN VIRAL TUMOR--MOLLUSCUM CONTAGIOSUM. (Ch.) Hung, T. (Dept. Virol., Chinese Acad. Med. Sci., Peking). Wei Sheng Wu Hsueh Pao (Acta Microbiol. Sinica) 9(3):203-209, 1963.

Various methods, including cortisone treatment, proved unsuccessful in an attempt to infect laboratory animals with the human molluscum contagiosum virus, but proliferation and infiltration, as well as the formation of inclusion bodies, were noted in the epidermal cells of inoc. chorioallantoic membrane and the skin of rabbits; rabbits intracerebrally inoc. with the virus showed cyst-like inclusions in the cytoplasm of the neurons. The studies appear to confirm the process of gradual inclusion body formation and dynamic changes of RNA and DNA in epidermal cells.

4-317 ELECTRON MICROSCOPIC STUDIES OF A HUMAN VIRAL TUMOR--MOLLUSCUM CONTAGIOSUM. (Ch.) Hung, T. (Dept. Virol., Chinese Acad. Med. Sci., Peking), C.-F. Pang and C.-Y. Hou. Wei Sheng Wu Hsueh Pao (Acta Microbiol. Sinica) 9(3):210-219, 1963.

Electron microscope studies of ultrathin sections of human dermal cells infected with the virus of molluscum contagiosum showed 3 stages in the development of the viral particles: an early granular form, an intermediate granular membranous form and a later mature form. Nuclear changes in the early stage included foliation of the nuclear membrane and the formation of pseudopod-like protrusions with karyoplasmic and cytoplasmic protrusions at the ends. Paralleling the nuclear changes, the cytoplasm showed some dense areas with masses of cytoplasmic substrate which may serve as a basis for the origin of the virus. A discussion follows on the probable cause of these changes and on the nature of the capsule and septum of the virus inclusions.

4-318 INHIBITION BY 5-IODODEOXYURIDINE OF THE ONCOGENIC EFFECTS OF ADENOVIRUS TYPE 12 IN HAMSTERS. (E.) Huebner, R. J. (Nat. Inst. Allergy Infectious Dis., Bethesda, Md.), W. T. Lane, A. D. Welch, P. Calabresi, W. McCollum and W. H. Prusoff. Science 142: 848-490, 1963.

Hamsters were inj. s.c. with 0.04 ml of diluted human adenovirus 12 (approx. 10^7 TCID₅₀/0.1 ml) within 24 hr. of birth and then treated immediately or 2 hr. later with 5-iododeoxyuridine (UdR; 0.5 mg x 1 at the same s.c. site), 14/34 developed tumors (10 died) during a 90-day period of observation. With virus + UdR immediately + 10 additional doses (on alternate days, the same or different s.c. site), tumor incidences were 8/37 (5 died); when the drug was given 24 hr. after + 9 additional doses, tumors occurred in 11 (5 died). Virus only controls showed tumors 26/28 (15 died). Virtually all tumor-bearing animals (despite UdR treatment) developed complement-fixing antibodies to adenovirus type 12 viral antigen; these antibodies were not found in animals which did not develop tumors.

64-319 TUMORAL DISEASE OF THE MOUSE TRANSMITTED THROUGH CELL-FREE MATERIAL. II. EVOLUTION OF THE DISEASE TOWARD A LEUKEMIC AND ALEUKEMIC FORM OF RETICULOSIS. (Rum.) Ilie, B. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest). Stud. Cercet. Inframicrobiol. 14(3):355-361, 1963.

A mouse tumoral disease (see CRA 2(2):#320, 1964), maintained for 10 mo. thru serial passages in mice, started as a tumor with ascites and hepatosplenomegaly, the latter becoming more predominant after several mo., with reticulosis of marrow, liver, spleen, intestinal lymph nodes and with appearance of peripheral blastic forms in some cases. Despite some similarities to the disease described by Friend and Metcalf, this tumor started as a predominantly carcinomatous involvement; leukocytosis was moderate and more than the spleen was involved. It developed in H mice where the incidence of leukemia is below 1%. It is also different from the disease produced by the polyoma virus not only morphologically, but also serologically (i.e., cold hemagglutination reactions both with guinea pig cells and with human O cells were negative).

64-320 TUMORAL DISEASE OF THE MOUSE TRANSMITTED THROUGH CELL-FREE MATERIAL. III. PRODUCTION OF LYMPHOID LEUKEMIA BY A CELL-FREE FILTRATE AND OF A TUMORAL ASCITES BY A PURIFIED CELL-FREE FRACTION. (Rum.) Ilie, B. (Inst. Inframicrobiol., Acad. Sci. Rumania, Bucharest). Stud. Cercet. Inframicrobiol. 14(6):777-782, 1963.

Cell-free splenic and hepatic filtrates, and/or Seitz filtered ascites, or filtrates purified by differential centrifugation from tumor-bearing mice (tumor 62) were inoc. i.p. in over 300 adult H mice of both sexes. Malignant tumors (carcinoma, ascites, and reticulosarcoma) were observed to develop in the course of several mo. and in a number of cases there was hematopoietic involvement (lymphoid hyperplasia, splenomegaly, extramedullary erythropoiesis, mild leukocytosis). The first case of typical lymphoid leukemia appeared 17 mo. after the start of the tumor 62 transplantation, in a mouse inoc. 5 mo. previously with splenic filtrate; generalized adenopathy, splenomegaly, and massive lymphoid infiltration of the liver were seen. A second mouse, in addition to these symptoms, showed a massive tumor of the thymus. Blood from the first mouse when inoc. i.p. into other animals produced the appearance of the same disease in 2/8, with generalized adenopathy and hepatosplenomegaly, in 1 mo. A second thymic tumor along with lymphoid leukemia appeared in a mouse 2 mo. after inoc. with a suspension of submaxillary lymph node cells from a tumor 62-bearing animal. When inoc. with cell-free soln. prepared by centrifugation, 3/6 developed ascites tumors (3 wk.), multiple mesenteric tumors (1 mo.) and a hepatic reticulum cell sarcoma (1 mo.). These are the first cases of ascitic tumors produced by inoc. of a cell-free extract of tumor 62.

- 64-321 PRODUCTION OF INTERFERON BY MONKEY KIDNEY CELLS INFECTED WITH SIMIAN VIRUS 40. (E.) Diderholm, H. (Inst. Virol., U. Uppsala, Sweden). Arch. Ges. Virusforsch. 14(1):39-44, 1963.

When kidney cells from the African green monkey (*Cercopithecus aethiops*) were infected with SV40, titers of the virus increased gradually during the 20 days of the test, while titers of an interferon-like product rose during 4-12 days and remained at the elevated level thereafter. Higher titers were obtained in stationary cultures or under more anaerobic conditions. This product inhibited the propagation of pseudorabies (Yugoslavian strain Z grown in mouse embryo cells) and poliomyelitis virus (LSc-2ab from monkey kidney cell cultures). Furthermore, as this inhibitor proved to be very sensitive to trypsin and ether and was partially inhibited by chloroform but was not sensitive to RNase, DNase or SV40 antiserum, and was neither dialyzable or sedimented by centrifugation, the author feels that it may be termed interferon.

- 64-322 MYXOVIRUS-LIKE PARTICLES IN ACUTE LEUKAEMIA. (E.) Editorial. Lancet 1:420, 1964.

The findings of A. J. Dalton et al. and M. Benyesh-Melnick et al. concerning virus particles in sera and plasma from children with acute leukemia were discussed and reviewed by J. L. Melnick and were found to be similar. Many myxovirus-like particles, 90-250 mμ in size with well-defined limiting membranes, were seen which were practically indistinguishable from murine and avian leukemia viruses, except that no 'tails' were demonstrated. In 24 children with leukemia, the serum and plasma samples were positive in 19 (79%), questionable in 1 and negative in 4 (10%); samples from 40 normal children showed 4 positive, 8 questionable and 28 negative, while all the samples from 13 adults were negative.

- 64-323 THE CARCINOGENIC ACTIVITY OF CELL-FREE EXTRACTS OF PS MOUSE TUMORS ON MICE OF DIFFERENT STRAINS. A NEW SERIES OF EXPERIMENTS. (Fr.) Mouriquand, C. (Nucl. Res. Ctr. Grenoble (CENG), France) and J. Mouriquand. Ann. Inst. Pasteur (Paris) 106(4):533-560, 1964.

Further observations are reported on the induction of tumors with cell-free extracts (CFE) of spontaneous mammary or induced leukemic tumors of PS mice (see CRA 1(3):#584, and ibid., (4):#718,

1963). CFE from lymphoblastic leukemic tumors (first passage in PS or Swiss mice) or from the culture medium of 6-day-old mammary explants were inj. i.p. into 256 newborn Gif male and female mice. Only 71/256 inj. animals survived to adulthood, 131 died before weaning and 54 before 6 mo. of age. Of the remaining 71, 6 males and 6 females (15.5%) developed malignancies which included 5 myeloid and 3 lymphocytic leukemias, 2 lymphosarcomas, 1 malignant plasmacytosis and osteoblastosarcoma. Two of the tumor-bearing mice had received inj. with CFE from the medium of a mammary tumor culture. Tumors appeared from 5.5-19 mo. In other experiments, mammary or leukemic tumor CFE were inj. i.p. into 160 newborn random-bred male and female mice. Of 57 which survived to maturity, 15 died between mo. 5-17 of various benign conditions; during the same period 26 (45.6%) died of malignancies which included 7 mammary tumors, 4 myeloid or 3 lymphoblastic leukemia, 1 reticulum cell sarcoma, 10 malignant plasmacytoses, and 1 hepatoma. Tumors appeared in 5-15 mo. Mammary tumors developed in mice receiving either mammary (2/7) or leukemic (5/7) tumor CFE. No relationship was observed between sex and type of tumors, with the exception that mammary tumors occurred only in females. These findings give further support to the theory of a viral origin of the spontaneous tumors of PS mice and suggest that the virus can reproduce in cultures.

- 64-324 ELECTRON MICROSCOPIC STUDY OF A MOUSE SPONTANEOUS TUMOR. THE PRESENCE OF VIRUS-LIKE PARTICLES. (Fr.) Hublet, C. (Dept. Path. Anat., U. Liege, Belgium) and H. Firket. C.R. Soc. Biol. 157(11):2111-2114, 1963.

Virus-like particles were found in 10-14-day-old Sarcoma J grown s.c. in C57BL mice. These particles occurred in the extracellular spaces as a budding of the tumor cell surface and consisted of a vesicular body 100-110 mμ in diameter enclosed in concentric triple membranes. The innermost membrane was the thickest of the three; the external membrane was continuous with the cytoplasmic membrane; the intermediate membrane was not always visible. Virus production varied from one cell to another but groups of 10 to 20 particles each were frequently observed; the same cell could present several protrusions of its membrane, each one supporting a group of viruses. Morphologically these viruses resembled the type C virus described by Bernard. They were found in all the animals inj. with tumor cells from different passages even at intervals of several mo. No virus-like particles were seen in the spleen and lymph nodes of the tumor-bearing mice.

See also abstract nos.: 167, 168, 169, 178, 185, 186, 189, 190, 191, 192, 206, 248, 249, 253

EPIDEMIOLOGY AND BIOMETRY

- 64-325 AIR POLLUTION IN THE REGION OF LIEGE. RESULTS OF A FOUR-YEAR STUDY ON THE CONCENTRATION OF RESPIRABLE PARTICULATES AND POLYCYCLIC HYDROCARBONS. (Fr.) Rondia, D. (Dept. Toxicol., U. Liege Sch. Pharm., Belgium). *Arch. Belg. Med. Soc.* 21(9-10):578-613, 1963.

An extensive paper describing the results of the determination (by filtration on paper discs) of the air conc. of smoke and polycyclic hydrocarbons in 12 representative sites of the Liege area (including urban, rural and industrial zones) during the various seasons of the year and the influence of several environmental factors (wind, rain, fog, topography, etc.) upon these conc. While smoke pollution follows an industrial pattern, polycyclic hydrocarbons appear to be related to sources of heat. No relationship could be established between the conc. of polycyclic hydrocarbons and the incidence of lung cancer in a given zone.

- 64-326 ROLE OF GASTRIC ULCER IN THE CAUSATION OF GASTRIC CANCER IN JAPAN: A HISTOPATHOLOGICAL STUDY OF 3,000 GASTRECTOMY MATERIALS. (E.) Oota, K. (Dept. Path., Tokyo Med. Dent. Coll., Japan). *Acta Un. Int. Cancr.* 19(6-7):208-1209, 1963.

In an examination of 2995 gastrectomy specimens collected during the past 14 yr., 1788 showed cancer of the stomach. Malignant transformation of gastric polyps was seen in less than 5%. Benign chronic ulcer scars in the stomach (independent of cancer) were seen in 61/1788 and linear ulcers (at the ends of which cancers were found to be present) occurred in 32/1788. Cancers of less than 2 cm in diameter with almost exclusive mucosal involvement were detected in 87/1788. Of these 187, 70% (90) were associated with chronic ulceration presenting signs of repair preceding development of cancer *in situ*; 7 cases showed the existence of linear ulcers and/or scars running into small cancers. About 45% of the cases showed scarring in the submucosal layers only, and in the remainder of the cases, the scars involved the innermost layers of the muscle. The scirrhous variety of gastric cancer was seen in 30% of the cases. The data indicates that not only chronic ulcers but rather shallow peptic defects of the gastric lining have a definite correlation with subsequent development of malignant neoplasms at the same site.

- 64-327 IMPROVEMENT OF THE EARLY DIAGNOSIS OF MALIGNANT CHANGES OF THE STOMACH. (Ger.) Gibel, W. (Robert-Rössle Clin., German Acad. Sci. Berlin). *Zschr. Aerzt. Fortbild. Jena* 58(1):1-7, 1964.

In a review (111 references) of recent efforts to

improve early diagnosis and/or prophylaxis of cancers of the stomach, the author concludes that chronic atrophic gastritis and both hypo- and anacidity are significant predisposing factors. Pernicious gastric achylia is found 21 times more frequently in pts. with gastric carcinomas than in pts. without gastric malignancies. Other predisposing factors are said to include gastric polyps and chronic ulcer ventriculi.

- 64-328 CANCER AND DISEASES PRECEDING CANCER OF THE STOMACH. (E.) Elansky, N. N. (Fac. Clin. Surg., 1st Moscow Med. Inst., USSR). *Acta Un. Int. Cancr.* 19(6-7):1172-1174, 1963.

Based on the analysis of 2729 pts. with cancer of the stomach, 1805 pts. with ulcers, and 367 pts. with stomach polyps seen over a 15-yr. period, the author feels that gastritis, ulcers, polyps, and cancer of the stomach are separate stages of a single pathological process. Of the pts. who had stomach cancer, 34.2% showed no previous stomach disease; 65.8% showed symptoms of malignant growth following long periods of various diseases of the stomach: 56% previously had achylia gastritis, 6.7% had stomach ulcers and 3.1% had formerly been treated for polyps of the stomach. Histological observation showed transformation of 7-10% of ulcers into cancer. Histological examination of 235 stomach polyp specimens after resection showed a transition of polyps into cancer or a simultaneous combination of both in 24.2% (57 pts.); cancer developed in 18/85 pts. who had polyps but were not operated on. Anatomical changes that occurred in the mucous membrane of the cancerous stomach were similar to those changes found in gastritis. Repeated operations for polyps of the stomach fixed the period of transition to malignancy at 5-10 yr. or longer in some cases.

- 64-329 INCIDENCE OF MALIGNANT MELANOMA. A STATISTICAL ANALYSIS OF 1629 CASES FROM THE STATISTICS ON CANCER PATIENTS OF THE GERMAN DEMOCRATIC REPUBLIC. (Ger.) Wildner, G. P. (Inst. Path., Humboldt U., Berlin). *Arch. Geschwulstforsch.* 22(1-2):71-80, 1963.

Among the total of 47,792 registered new cancer cases in the German Democratic Republic in 1959, only 553 cases (1.2%) were malignant melanomas. The present work is a statistical analysis of 1629 new malignant melanoma cases registered between 1953-1956. Among these pts., the primary tumor site could not be determined in 59/1629 cases (3.6%). Of the remaining 1570 cases, the chief primary sites were: skin (1230 = 78%); eyes (302 = 19%); mucous membranes of upper digestive and respiratory tract (12 = 0.8%); rectal mucous membranes (10 = 0.6%; not including 2 cases involving the anal region and classified under the skin involvement). Malignant melanoma of skin and eyes (97% of all pts.) were analyzed in detail

as to age and sex distribution (skin melanomas were also tabulated by site in great detail). After age 25 yr., the incidence of malignant melanoma of the eye rose with increasing age both in men and women, but the incidence was markedly higher in 65-75-year-old men than in women of that age. After the age of 5 yr., incidence of malignant melanoma of the skin also rose with increasing age, and was higher in 20-45-year-old women than in men of that age. Among the skin melanomas, 32% involved the head and neck (with 40% of these present on the cheeks), 13% involved the upper extremities, 25% the lower extremities, 28% the trunk, 2% the genitals. It was concluded that among other factors, hormones and sun rays may play a role in the genesis of malignant melanoma.

- 64-330 CANCER IN AN AFRICAN COMMUNITY, 1897-1956. AN ANALYSIS OF THE RECORDS OF MENGO HOSPITAL, KAMPALA, UGANDA: PART 2. (E.) Davies, J. N. P. (Albany Med. Coll. Union U., Albany, N.Y.), S. Elmes, M. S. R. Hutt, L. A. R. Mtimavalye, R. Owor and L. Shaper. *Brit. Med. J.* 1:336-341, 1964.

After an analysis of the records available since 1897 from Mengo Hospital, it was concluded that cancer in Uganda for over 60 yr. has been as common as it is today and has the same general distribution. The following statistics were given comparing incidences of some cancers from the total statistics for Mengo Hospital (MH) and more recent figures from the Kampala Cancer Registry (KCR): ovarian carcinoma (11.6% MH, 8.7% KCR); vagina and vulva (2.2% MH, 3.2% KCR); breast, male (0.9% MH, 0.5% KCR); breast, female (10.4% MH, 9.2% KCR); cervix uteri carcinoma (22.9% MH, 24.5% KCR); penis (14.9% MH, 12.2% KCR). Based on the percentage of all cancers, the following comparisons were made: stomach (4.3% MH, 2.8% KCR); colon (4.3% MH, 1.3% KCR); pancreas (1.8% MH, 0.6% KCR); ovary (5.9% MH, 3.6% KCR); primary and secondary liver cancer (7.9% MH, 8.0% KCR); leukemias (2.1% MH, 3.2% KCR); myelomas (0.2% MH, 0.5% KCR). However, when the percentage was based on all the leukemias in MH and KCR, lymphatic was 35% and 41.3%; myeloid, 60% and 48.8% and unclassified acute, 5.0% and 9.9%, resp. Statistics for tumors of the bone, jaw, eye and orbit as well as soft-tissue sarcomas and tumors in children for the MH are also given. After a steady decline for 6 decades, lip cancer today is uncommon and represents the only genuine change in the cancer pattern. The percentage of children (15 yr. and under) with cancer showed a slight fall; tumors of the jaw and eye/orbit constitute 33% of the total. (See also the following abstract.)

- 64-331 CANCER IN AN AFRICAN COMMUNITY, 1897-1956. AN ANALYSIS OF THE RECORDS OF MENGO HOSPITAL, KAMPALA, UGANDA: PART 1. (E.)

Davies, J. N. P. (Dept. Morbid Anat., Postgrad. Sch. Med., London), S. Elmes, M. S. R. Hutt, L. A. R. Mtimavalye, R. Owor and L. Shaper. *Brit. Med. J.* 1:259-264, 1964.

As indicated in CRA 2(2):#330, 1964, the incidence of cancer in Mengo Hospital (in relation to total admissions) has been rather stable over the last 6 decades (1897-1956) and has totaled 965 cases (0.91%) of 107,272 admissions. Cancer by site (number of cases and percentage of total) are also recorded over the same period along with comparable figures from the Kampala Cancer Registry (KCR). All Mengo Hospital cases from 1952-1956 were included in the figures of the KCR for 1952-1960.

- 64-332 STATISTICS ON CAUSES OF MORTALITY. (Ger.) Zschoch, H. (Inst. Path., U. Leipzig, Germany). *Deutsch. Gesundh.* 19(7): 311-314, 1964.

The most frequent cause of death in the German Democratic Republic in yr. 1960 among a total of 5485 autopsies was due to malignancies, 32% of all deaths (carcinoma, 28.13%, sarcoma; 1.74% and hematological cancer 2.13%). Heart and circulatory diseases were in second place and account for 31.24% of all deaths.

- 64-333 MORTALITY AND ENVIRONMENTAL FACTORS. MORTALITY IN VARIOUS DISEASES IN RELATION TO THE TIME OF DAY. (It.) Pino Saccà, F. (Inst. Anat., U. Rome), G. Mauro and G. Cardellino. *Minerva Med.* 55(1-2):17-23, 1964.

An analysis of the data accumulated over a period of 16 years (1937 to 1952) at the Hospital of St. John the Baptist and by the City of Turin showed that of 2123 deaths due to neoplastic diseases, 49.84% occurred during the first part of the day, that is from 1 a.m. to 12 noon and 50.16% from 1 p.m. to midnight. For the same diseases, the percentage mortality at 1, 3, 5, 7, 9, 11 a.m., was, resp., 9.1, 5.3, 9.1, 7.2, 8.1 and 10. Mortality at 1, 3, 5, 7, 9, 11 p.m., was, resp., 8.6, 9.3, 8.9, 7, 7.4 and 7.9. Similar figures are tabulated for tuberculosis, nephropathy, heart disease, infectious diseases, cerebrovascular diseases, and for diseases of the respiratory and the gastrointestinal system.

- 64-334 THE RELATIONSHIP BETWEEN THE DETERMINATIONS OF TUMOR FREQUENCY AND PROBABLE TUMOR ETIOLOGY. (It.) L'Eltore, G. (Sch. Health Statistics, U. Rome). *Minerva Med.* 55(1-2): 6-11, 1964.

A comparative study of the official statistics of 22 countries shows that cancer mortality has in general doubled or tripled from 1900 to date. Countries such as Denmark, Switzerland, France, Sweden, The Netherlands, and Norway, which already

At the beginning of the 20th century had a high standard of living and a high tumor mortality, presented in 1960 the lowest relative increase (2.8-86.5%). On the other hand, countries such as Austria, Belgium, England, Scotland, Germany, and Hungary, which had low tumor incidences, in 1960 presented some of the highest increments observed (160-357%). In the remaining countries (Finland, USA, Italy, New Zealand, Australia, Japan, Spain, Portugal, Venezuela, and Colombia) changes of tumor mortality had unique characteristics due to the different demographic structure and the different degree of medicine and public health organization. Within this period, when the tumor incidence had attained its peak value, it often became stabilized within a certain range, presenting thereafter only moderate increases, which were ascribed more to improved diagnostic methods and to the increase in the population of people in the older age group (over 55 yr.) than to a real increase. The curve representing the phenomenon of tumor incidence over the years was very similar to that observed with infectious diseases, thus suggesting a possible role of viruses in carcinogenesis. In relation to site it was found that gastric and uterine cancer mortality decreased 7.3 and 18%, resp., from 1950 to 1960, whereas in the same period leukemia, bronchopulmonary, prostatic and mammary carcinoma showed an increase of 28, 18, and 7%, resp.; no significant changes were observed for other sites. In Italy in 1957, 1% of tumor deaths were due to stomach cancer, 1% to cancer of the liver and biliary ducts, 1% to intestinal tumors, and 8.4% to bronchopulmonary forms. According to occupation 23% of these pulmonary forms occurred in factory workers, machine operators and in personnel with technical and administrative duties; the incidence in other categories was lower. Mortality due to stomach cancer was over 32% in farmers and fishermen, and 24% in industrial workers, retired people, well-to-do people, and tradesmen. Mortality due to cancer of the liver and biliary ducts had similar frequencies in all occupational groups examined.

64-335 SOCIOCULTURAL ASPECTS OF CERVICAL CYTOLOGY IN ALAMEDA COUNTY, CALIF. (L. Breslow, L. (California State Dept. Public Health) and J. R. Hochstim. Public Health Rep. 79(2):107-112, 1964.

Use of the cervical cytological test (Papanicolaou test) in Alameda County has been profoundly influenced by sociocultural factors: women in minority racial and ethnic groups of low socioeconomic status made least use of the test, although these same groups showed the highest incidence of cervical cancer. Of the 266 cases of cervical cancer reported to the Alameda County cancer registry for 1960, 205 (77%) were white, 41 (15%) were Negroes, and 20 (7%) were other races; the relative proportions of the 3 groups according to the 1960 census was 86%, 11% and 3%.

Among women diagnosed as having cervical cancer, the proportion of Negroes, aged 20-29, was twice (10%) that of white women (5%) in the same age group.

64-336 SQUAMOUS CELL CARCINOMA ARISING IN A PILONIDAL SINUS. (E.) Cleveland, B. R. (Dept. Surg., U. Texas Med. Branch, Galveston) and W. O. Green, Jr. Surgery 55(3):381-386, 1964.

The author presents a well documented case of a 32-year-old man with squamous cell carcinoma arising in a pilonidal sinus. This is the second case presenting sacrococcygeal involvement of the 12 cases previously recorded in the literature (4 foreign, 8 American) and summarized by the author (13 references).

64-337 INTRA-EPITHELIAL CARCINOMA OF THE UTERINE CERVIX. (E.) Wahi, P. N. (Dept. Path., S.N. Med. Coll., Agra, India), U. Kehar, S. Mali and O. P. Bansal. Acta Un. Int. Cancr. 19(6-7):1379-1383, 1963.

Among 4189 cases of various benign and malignant lesions of the cervix uteri, the percentage of pts. with various lesions was: basal cell hyperplasia, 1.3%; intra-epithelial carcinoma, 1.6%; invasive carcinoma, 29.9%; chronic cervicitis, 40.6%; erosion cervix, 16.8%; cervical polyp, 6.9%; epithelial dysplasia, 2.9%. For various lesions, the av. age and number of pts. was: basal cell hyperplasia (34.2 and 50), epithelial dysplasia (36.3 and 125), intra-epithelial carcinoma (37.7 and 64) and invasive carcinoma (45.6 and 1256). This ascending trend in age is believed to be of considerable significance in understanding the pathogenesis of cervical carcinoma. The initial symptoms in the pts. with intra-epithelial carcinoma and the precancerous epithelial atypias were almost similar. The majority of cases of intra-epithelial carcinoma showed insignificant gross alterations; 17.2% showed a healthy looking cervix, 54.7% were diagnosed as non-neoplastic cervical lesions, and the remaining 28.1% as cervical erosion suspicious of malignancy. All the pts. were married (12.5% widowed) and 64.1% were married between 13-16 yr.; 12.5% were nulliparous and 71.9% had given birth to their first child at the age of 14-19 yr. and 60% of these pts. had 3-8 children.

64-338 SKIN MALIGNANCY IN MINORS. (E.) Perrett, L. (Queensland Radium Inst., Brisbane, Australia). J. Coll. Radiol. Aust. 6(1):37-41, 1962.

Of 35,000 cases of skin cancer treated by the author since 1940, there were 152 cases in persons under the age of 21 yr. (77 basal cell and 37 squamous cell carcinomas and 38 cancers of the lip); the youngest pt. was a 5-year-old child

with squamous cell carcinoma of the nose, but the majority were nearer 21 yr. of age. The sex (male and female) distribution of 240 pts. with cancerous and pre-cancerous lesions of the skin and lips in children was: keratoses, 66 and 22 (youngest pt. was age 9 yr.); squamous cell carcinoma, 25 and 12; basal cell carcinoma, 42 and 35 (youngest age 7 yr.); all lesions of the lip, 36 and 2 (youngest age 9 yr.), resp. In Queensland the incidence (per 1,000,000 of population) of skin cancer is 3500 in Brisbane, and in Townsville (900 miles further north) 8000. For comparison, rates in Detroit, Pittsburgh, New Orleans and Dallas are 240, 370, 1290 and 1400, resp. Precautions are advised against excessive exposure to the sun.

- 64-339 ARSENIC AND SKIN CANCER. (E.) Sanderson, K. V. (St. George's Hosp., London, S.W.1). Trans. St. John's Hosp. Derm. Soc. 49(2):115-122, 1963.

The history of the association between arsenic and skin cancer is reviewed (31 references). Ten illustrative case histories were given of pts. treated with various arsenic preparations (total dose not stated) for various noncancerous diseases. All the pts. developed various types of skin carcinomas (intraepidermal, squamous cell, basal cell; 1 or more) as well as an anaplastic bronchial carcinoma in 1/10. The latent period between the start of arsenic treatment and the appearance of malignant changes varied from 4 yr. in 1/10 to more than 30 yr. in 2/10. Various other hyperplastic changes of the skin also occurred.

- 64-340 KAPOSI'S SARCOMA. (E.) Davies, J. N. P. (Dept. Path., Albany Med. Coll., N.Y.). Trans. St. John's Hosp. Derm. Soc. 49(2):93-98, 1963.

In a discussion on Kaposi's sarcoma the author describes clinical studies, symptoms, histology and histopathology of the disease. As to geographic distribution, the disease is especially common in the northeast region of the Congo basin and frequency tends to fall as the desert belts are reached. The distribution of nodules in 192 Ugandan cases was greatest in the lower limb (85.4%) and least in the gum, salivary gland and pharynx (total, 0.5%). On the basis of autopsies performed on 19 cases, lymph nodes and the skin were the major organs most affected (both 73.7%), while the salivary gland was the least affected (10.5%). The crude rates of Kaposi's sarcoma (per 100,000/yr.) in male Ugandans, U.S. whites, and U.S. Negroes, were resp., 2.6, 0.081 and 0.103. In Uganda the disease is common enough to show age specific rates. There is a small peak in childhood followed by a fall in the teens with the rate rising steadily with age thereafter. In 10 male Ugandan children (age 18 mo.-12 yr.), the sarcoma was found most often in the cervical lymph nodes (7).

- 64-341 EPIDEMIOLOGY OF CHILDHOOD LEUKAEMIA IN NORTHUMBERLAND AND DURHAM. (E.) Knox, G. (Dept. Child Health, U. Newcastle/Tyne, England). Brit. J. Prev. Soc. Med. 18(1):17-24, 1964.

In 185 cases of leukemia in children under 15 yr. in Northumberland, Durham and Tees-side over a 10-yr. period (1951-1960), a higher risk was seen in children of larger towns as shown by the following: lymphoblastic--urban 88/185, rural 55/185; myeloblastic--urban 33/185, rural 13/185. There were 109 males, 76 females (3:2 ratio). Mean age of onset for the myeloblastic leukemias which occurred before age 15 was 7.7 yr.; for lymphoblastic leukemia this was 5.82 yr. in large towns and 4.5 yr. in other areas. As to seasonal variation, 111/185 clinical onsets occurred in the summer, against 74/185 in the winter; with summer to winter onsets of 84 to 55 and 27 to 19 for lymphoblastic and myeloblastic types, resp. Excluded were approx. 11% of the 6-year-old children presenting abnormal karyotypes, 9/185 mongols, 1/185 "slightly mongoloid", and 11/185 children with irradiation history either in utero or later. Evidence of a clustering factor, a space-time interaction, in children under 6 yr. with lymphoblastic leukemia was observed in 5 very close pairs, closer than 60 days in their dates of onset and closer than 1 km on the map. There was no evidence of maternal age or birth rank variations of risk apart from the association with mongolism.

- 64-342 INCIDENCE OF THE BURKITT TUMOUR IN IBADAN, WESTERN NIGERIA. (E.) Edington, G. M. (Dept. Path., U. Ibadan, Nigeria) and C. M. U. Maclean. Brit. Med. J. 1:264-266, 1964.

The crude and age-specific rates of the Burkitt tumor in Ibadan, Western Nigeria were assessed over a period of 3 yr. Out of a total of 1,934 malignant tumors recorded over yr. 1960 through 1962 in the Ibadan Cancer Registry, 230 occurred in children 0-14 yr. old; the Burkitt tumor represented 70% of the neoplasms. Based on the age-specific rate per 100,000 of Ibadan population (April 1960-March 1963), the Burkitt tumor was found to be most common in 5-9-year-old males and 10-14-year-old females. Comparison studies showed the tumor to be the most common malignancy in children, being many times more common than leukemia in the American Negro in comparable age groups. When all age groups are considered, the Burkitt tumor has been the second commonest form of malignant disease to be diagnosed in Ibadan in recent years, being exceeded in frequency only by carcinoma of the uterine cervix.

- 64-343 AGE INCIDENCE IN BURKITT'S LYMPHOMA SYNDROME. (E.) Haddow, A. J. (E. Afr. Virus Res. Inst., Entebbe, Uganda). E. Afr. Med. J. 41(1):1-6, 1964.

To determine whether an arthropod-borne virus was

the causative agent of Burkitt's lymphoma syndrome, the author has made an analysis of age distribution in Burkitt's series of 363 cases from various African communities (Uganda, Tanganyika, Mozambique and Nigeria). Though 5 scattered cases of the syndrome were reported, only 6 were older than 20. It was noted that the fraction of the population which stands at the risk of responding to the postulated infection (by development of the tumor) has been virtually eliminated by age 20. The cumulative age-incidence showed that up to age 6-7, the absolute incidence increases by a mean of 60%/yr. (very roughly), and above this age about 25% of the population at risk is affected in each succeeding year. The jaw and orbit are a particularly common site for the tumor among African children, but tumors are frequently found in other sites. In males and females, the highest incidence of jaw and orbit tumors occurred in the 4-8-year age group with the median for both sexes being 6-7 yr., while the peak incidence of non-jaw tumors in males occurred at age 7-8 yr. and in females at age 8-9 yr. While no definite conclusions could be drawn from this study, the author felt that if the causative agent was a virus and the infection a common one, then many children would be born with a passive immunity lasting from 6-12 mo.; later, however, when the children began to roam about independently (starting at about age 3), then the main rush of cases would begin.

4-344 CARCINOMA OF THE SCROTUM IN A TIRE RECAP WORKER. (E.) Larkin, J. C., Jr. Dept. Pulm. Dis., VA Med. Teaching Group Hosp., Memphis, Tenn.), W. T. Murdock and S. Phillips. Arch. Derm. 89(2):247-249, 1964.

A case is reported of a 35-year-old Negro man with carcinoma of the scrotum, who 6 yr. previously was employed in a tire recapping plant for 9 mo. During his employment, the pt's. trousers frequently became soaked with a rubber solvent of undetermined nature. A crude rubber cement and kerosene are also employed in the work. It was speculated that in an inadequately vulcanized recap, carbon black might be released by buffing, or leached out by solvent. While carbon black contains such carcinogens as 3,4-benzopyrene, no definite conclusions were drawn from this case.

4-345 FAMILIAL FACTORS IN HUMAN LUNG CANCER AND SMOKING. (E.) Tokuhata, G. K. St. Jude Res. Hosp., Memphis, Tenn.). Am. J. Public Health 54(1):24-32, 1964.

see CRA 1(1):#128, 1963.

4-346 LUNG CANCER AND MONTH OF BIRTH. (E.) Allan, T. M. (Royal Infirm., Aberdeen, Scotland). Lancet 1:439-440, 1964.

In a discussion of papers from The Netherlands (see CRA 1(9-10):#1772; *ibid.*, (12):#2181 and #2211, 1964) and England (see CRA 1(12):#2180, *ibid.*, 2(2):#347, #348, and #349, 1964) on the incidence of lung cancer and the month of birth, the author notes that the differences between the 2 series may be due, at least partially, to environmental differences, and that many more series will be needed before a definite conclusion can be made.

64-347 LUNG CANCER AND MONTH OF BIRTH. (E.) Loxton, G. E. Lancet 1:217-218, 1964.

The author reports his statistical analysis of previously reported papers which indicated that there was no variation between the mo. of birth and the incidence of lung cancer as compared to Dijkstra (see CRA 1(9-10):#1772, 1964), who found increased susceptibility to lung cancer in people born later in the winter. A highly significant variation was seen in Davies series (see CRA 1(12):#2180, 1964) in the mean number per mo. born in August and September (187) as compared to the other mo. of the yr. (166.8; difference of means = 20.2, $t = 4.7$, $P < 0.001$) and in Baas and Strackee's series (see CRA 1(12):#2211, 1964) where there were more cases born from January to April per mo. (121.3) than in the 4 adjacent mo. of November, December, May or June (99.3/mo.). When the figures of v.d. Wal (see CRA 1(12):#2181, 1964) were added to those of Dijkstra, the mean relative incidence for February and March was 1.23 as compared to a mean relative incidence of 0.80 for the 6 adjacent mo. The author notes that he obtained different figures because he used different statistical procedures than the other authors. (See also CRA 2(2):#346, 1964.)

64-348 LUNG CANCER AND MONTH OF BIRTH. (E.) Jones, I. Lancet 1:47, 1964.

Of 95 pts. with carcinoma of the lung, the incidence of cancer based on the mo. of birth was: January = 4; February = 10; March = 9; April = 8; May = 12; June = 9; July = 9; August = 6; September = 8; October = 7; November = 7; December = 6, resp. There was no definite correlation in this series of lung cancer and mo. of birth. (See also CRA 2(2):#346, 1964.)

64-349 LUNG CANCER AND MONTH OF BIRTH. (E.) Loxton, G. E. Lancet 2:1385-1386, 1963.

A study of the relative incidence of astrocytoma of the cerebrum based on the season of birth showed: 1.09 incidence for 69 pts. born in Jan.-Feb.; 1.10 for 75 pts. born in March-April; 0.85 for 53 pts. born in May-June; 0.88 for 62 pts. born in July-Aug.; 0.93 for 60 pts. born in Sept.-Oct.; 1.12 for 70 pts. born in Nov.-Dec. Therefore, pts. with astrocytoma of the cerebrum are

more likely to be born in the mo. of Nov.-April (mean relative incidence of 1.103) than in the mo. of May-Oct. (mean relative incidence of 0.886). No seasonal incidence based on the mo. of birth was found in 741 pts. with bronchial carcinoma, although it did appear that more pts. with bronchial cancer are born from July-Oct. than during the rest of the year. It was noted that these results do not coincide with the findings of Dijkstra's (see CRA 1(9-10):#1772, 1964).

- 64-350 LUNG CANCER AND MONTH OF BIRTH. (E.)
Davies, J. M. (Royal Marsden Hosp.,
London, S.W.3). Lancet 2:1283, 1963.

See CRA 1(12):#2180, 1964.

- 64-351 THE INCIDENCE OF MALIGNANT TUMORS OF
THE URINARY SYSTEM. NOTE II. A
SURVEY CONDUCTED AMONG VARIOUS ITALIAN UROLOGY
DEPARTMENTS. (It.) Tana, E. (Dept. Urol.,
Riuniti Hosp. St. Antonino, Florence, Italy).
Urologia (Treviso) 30(6):605-612, 1963.

Among a total of 1,989 pts. with urinary conditions observed during yr. 1957-1961, 183 (9.72%) had malignant tumors of the urinary system (including prostate and seminal vesicles), 415 (21%) benign hyperplasia of the prostate and sclerosis of the bladder neck, 70 (3.5%) benign papillomas, and 330 (17.1%) primary calculosis. Incidence by site relative to total malignant tumors was: renal parenchyma, 13.6%; renal pelvis, 0.5%; ureters, 1.6%; bladder, 49.5%; prostate, 34.9% and urethra, 0%. When the author's data were combined with data from the urology departments of 8 other Italian hospitals (yielding a total of 43,106 pts.) the incidence of malignant tumors in the entire group was 6.3% while the relative incidences for the same sites were, resp., 13.53%, 1.47%, 1.21%, 41.9%, 39.8% and 2.43%.

- 64-352 FIVE CASES OF MALIGNANT ADENOMA OF THE
THYROID FOUND IN ONE FAMILY. (Jap.)
Harano, A. (Dept. Surg., Nagasaki U. Sch. Med.,
Japan), T. Miura, Y. Ando, S. Yamamoto. Nagasaki
Igakkai Zasshi (Nagasaki Med. J.) 38(2):182-183,
1963.

Familial aggregation of 3 malignant adenomas of the thyroid and 2 questionable malignant adenomas of the thyroid is reported. Among 13 siblings with healthy parents, two sisters (age 36 and 27) were diagnosed as having adenocarcinoma of the thyroid and a 20-year-old sister was also diagnosed as having a questionable malignant change of the thyroid. A 29-year-old brother was diagnosed as having adenocarcinoma of the thyroid with regional metastases; a 9-year-old daughter of this pt. has a congenital goiter which is being followed by the authors because of suspicion of malignancy.

- 64-353 PIGMENTATED BASAL CELL CARCINOMA.
(II) STATISTICAL CONSIDERATION.
(Jap., Abstract) Miki, Y. (Osaka U., Japan).
Nippon Hifuka Gakkai Zasshi (Jap. J. Derm.)
73(8):550, 1963.

In an attempt to explain the higher incidence of pigmented basal cell carcinomas in males than in females in Japan, the records of 200 pts. were studied. In both males and females disease was seen earlier in those pts. with pigmentation compared to those without pigmentation. As to the involved area, there was no difference relative to exposure in males and females. Males exhibited many pigmented lesions which had been present for over 10 yr. while in females there were many non-pigmented lesions which appeared within 3 yr. When first inspected, the diameter of the tumors was greater in females than in males; the smaller tumors were more heavily pigmented.

- 64-354 SIGNIFICANCE OF PRECANCEROUS STAGE OF
JAPANESE GASTRIC ULCER. (Jap.) Okabe, H.
(Second Dept. Med., Kyushu Sch. Med., Japan). •
Fukuoka Igaku Zasshi (Fukuoka Acta Med.) 54(6):
699-708, 1963.

In a discussion of carcinoma of the stomach in relation to gastric ulcers, the author states that malignant degeneration of a benign ulcer would be extremely rare, if it occurs at all. Long term studies are needed to resolve this problem.

- 64-355 PATHOLOGICAL STUDY OF GASTRIC CANCER
ASSOCIATED WITH GASTRIC ULCER IN THE
JAPANESE. (Jap.) Imai, T. (Dept. Path., Cancer
Res. Inst., Kyushu U., Japan). Fukuoka Igaku
Zasshi (Fukuoka Acta Med.) 54(6):697-699, 1963.

In a study of surgical specimens from pts. with an early diagnosis of carcinoma of the stomach, concomitant gastric ulcer and stomach carcinoma was found in 60/73 (82.2%) Japanese and 31/45 (68.9%) Caucasians in the U.S. The author believes there is no basis for the presumed high incidence among the Japanese of preexisting gastric ulcer and any type of ulcerated carcinoma.

- 64-356 THE CANCERS OF THE GASTRIC STUMP AFTER
GASTRECTOMY FOR ULCER. (Fr.) Levrat, M.,
J. Pasquier and M. Croisille. Rev. Lyon Med.
12(12):691-702, 1963.

Reported are 9 pts. (8 males and 1 female) who were gastrectomized at age 28-56 yr. for an ulcer (duodenal, 5; gastric, 3; unknown site, 1) of benign nature. After an av. interval of 16 yr. (range 9-32 yr.) during which time the pts. remained asymptomatic, gastric cancer developed in all (av. age was then 58 yr.) and was localized at the anastomotic site in 4/9, at the upper pole in 2/9 while 3/9 had disseminated forms or the site could not be determined. The etiology,

athological anatomy, clinical and radiologic
ymptomatology, and diagnostic problems of these
orms of gastric cancer are discussed in relation
o 151 similar cases taken from the literature.

urvey of experimental data related to the
athogenesis of these forms demonstrates that,
ue to their rare occurrence, it is not possible
o determine whether the frequency of gastric
ancer is higher in gastrectomized than in nor-
al subjects. Thus the existence of a relation-
hip of causality between cancer of the gastric
tump and previous gastrectomy for gastroduodenal
lcer is difficult to establish. However, should
uch a relationship exist, carcinogenic stimuli
ay be postulated to include operative trauma,
astritis of the stump, or more likely (at least
ccording to the authors), the gastric anachlor-
ydia which is the usual consequence of an
ffective gastrectomy.

4-357 TWO NEW CASES OF SARCOMATOUS TRANS-
FORMATION OF GASTRIC ULCER. THE
RELATIONSHIP BETWEEN THE TUMOR AND THE CON-
CURRENT RETICULO-LYMPHATIC REACTIONS. (Fr.)
usy, J. P. (Path. Inst. U. Geneva, Switzerland).
n. Anat. Path. (Paris) 9(1):33-47, 1964.

ter a review of previously published cases (22
ferences) the author reports to have observed
autopsy in a woman and man (ages 88 and 83,
sp.) two reticulum cell sarcomas localized
round a chronic gastric ulcer; lymph node metas-
ses were not found. In addition, he describes
o cases (1 male and 1 female, both age 60 yr.)
o presented an unusually marked lymphoreticulo-
ic infiltration in the center of atrophic and
aplastic gastritis accompanied by subacute
cers which did not involve the muscular layers.
e lymphoreticulocytic proliferation was par-
cularly marked around the ulcer edges, present-
g epithelial and mesenchymal benign atypical
ils. The latter phenomenon was interpreted as
e expression of a "pre-sarcomatous" condition.

-358 EPIDEMIOLOGY OF CANCER OF THE STOMACH
IN JAPANESE. (Jap.) Kuratsune, T.
ept. Public Health, Kyushu U. Sch. Med., Japan).
kuoka Igaku Zasshi (Fukuoka Acta Med.) 54(6):
3-697, 1963.

review of literature referring to incidence of
d mortality from cancer of the stomach connected
th geographical, racial, occupational and social
ctors and habits in the world. According to
statistics for 1955 from the Ministry of Health
Japan, mortality for males in Japan is 4 times
gher than that of white Americans. Compared
the av. for all of Japan, incidence is 20%
gher in numerous parts of the northern pre-
ctures and is 50% lower in most of the southern
fectures. Mortality is also 1.10 and 1.11
es higher for males and females, resp., living
large cities (population $> \frac{1}{2}$ million) than in
er areas in Japan. In 1960 the mortality rate
er 100,000 population) from cancer of the

stomach in Japan was 57.3 and 34.6 in females
and males, resp., and this rate has not been sig-
nificantly altered since.

64-359 ON THE INCIDENCE OF LEUKEMIAS IN
HIROSHIMA DURING THE PAST 17 YEARS
FROM 1946 TO 1962. (Jap., Abstract) Watanabe, S.
(Dept. Path., Hiroshima U., Japan), F. Hirose,
K. Yokoji and S. Takizawa. Nippon Ketsueki Gakkai
Zasshi (Acta Hemat. Jap.) 26(3,4):441-442, 1963.

During 1962 there occurred 14 cases of leukemia
in Hiroshima; 8 of these pts. were exposed to the
atom bomb within 5,000 meters of the hypocenter.
Mortality in 1962 was 13, of these 7 were exposed
to the atom bomb blast. Total incidence of leu-
kemia during 17 yr. (1946-1962) was 288 cases; of
these 184 (acute type 107, chronic type 77) were
exposed to the atom bomb. For the same period
165/260 deaths were in individuals exposed to the
bomb. Leukemia was observed in 40 pts. who moved
into Hiroshima from outside of the city. Among
those who moved into Hiroshima within 1 wk. after
the blast, 33 pts. showed chronic leukemia; 28
pt. who entered within 3 days also developed the
chronic type of leukemia; only 1 pt. showed
chronic leukemia among 7 pts. with leukemia who
entered Hiroshima 3 yr. after the blast.

64-360 BRONCHOPULMONARY CARCINOMA IN VENICE.
(It.) Ferrari, E. (Inst. Anat. Path.,
United City Hosp., Venice, Italy), G. Fasan,
E. Forti and L. Rampinelli. Riforma Med. 77(43):
1197-1201, 1963.

In Venice, a typical non-industrialized city,
25/100,000 people die each yr. of lung cancer.
During the past 10 yr. 21% of all pts. who died
of cancer (30% of all men) had bronchopulmonary
carcinoma. The male:female ratio was 8:1. Among
100 men with lung cancer, 92% were smokers com-
pared to 71% in controls (200 men, 100 women);
among the smokers approx. 50% were heavy smokers
(20% in controls), sometimes with levels of con-
sumption as high as 60-80 cigarettes a day. Of
8 women with lung cancer, 5 were heavy smokers,
1 smoked moderately and 2 were nonsmokers (87%
of control women were nonsmokers and only 1 was a
heavy smoker). During the past 10 yr. the ratio
of small cell and squamous cell carcinomas has
increased to 4:1. Results of studies of tumor
type distribution among the authors' cases are in
agreement with the general belief that cigarette
smoking plays a role in the etiology of small cell
and squamous cell carcinomas. They are most fre-
quent in men, even in middle age, especially if
they are heavy smokers; adenocarcinomas, on the
contrary, are found in older pts. and not infre-
quently in women. Of 8 women with lung cancer,
6/8 smokers had squamous cell carcinoma and 2/8
nonsmokers had adenocarcinomas and were advanced
in age. As to occupation there were more glass
workers and painters in the cancer group than in
the control group. The characteristically uneven
climate of Venice, usually warm and humid but with

frequent changes to dry and cold weather, favors the development of respiratory diseases.

- 64-361 MORTALITY IN MEXICO CITY IN RELATION TO ECONOMIC CLASSES. (Sp.) Flores T., R., F. Pestaña C., J. Kahum G. and H. Novelo L. *Salud Publica Mex.* 5(6):865-868, 1963.

In a study of cancer deaths for 1962 in Mexico City, distribution according to "class" was: upper (av. income over 600 pesos/mo.) 30.4%; middle (av. income 300-600 pesos/mo.) 22.5%; lower (av. income less than 300 pesos/mo.) 15.3%. The high tumor mortality seen in the group with the highest standard of living is ascribed to better medical care and to the longer av. life span. The picture was similar for heart disease.

- 64-362 ON FAMILIAL OCCURRENCE OF GLIOMAS. (Ger.) Metzel, E. (Neurosurg. Clin., U. Freiburg/Br., Germany). *Arch. Psychiat. Nervenkr.* 204(6):537-555, 1963.

Three glioma cases are reported. In a case of ependymoma in a 9-year-old boy, family history revealed the same disease to have caused the death of a brother, while the mother had suffered from seizures and a grandmother had been psychiatrically "aberrant". In a 42-year-old male with an astrocytoma, it was ascertained that a brother had died of a brain tumor in a similar location. In a case of glioblastoma in a 29-year-old female, the mother and a brother were affected with Recklinghausen's disease. The possibility of a hereditary predisposition for this type of tumor is discussed; other familial and twin cases reported in the literature are compiled in tables and reviewed.

- 64-363 THE PROBLEM OF SYNTROPY OF LEUKEMIA AND CARCINOMA. (Ger.) Helbig, W. (Med. Clin., Karl-Marx-U., Leipzig, Germany) and K.-G. Voigt. *Arch. Geschwulstforsch.* 21(3):213-220, 1963.

In 9 pts. both leukemia (7 chronic lymphatic, 1 chronic myeloid, 1 acute) and carcinoma were observed. Diagnosis of the leukemia was prior to (2/9), simultaneous with (2/9), or subsequent to (5/9) the diagnosis of carcinoma; 6/9 had been treated by X-ray and/or cytostatics. The carcinomas by site included stomach 3, rectum 1, breast 2, uterus and cervix 2; 1 was a glioblastoma. Evaluation of autopsy material spanning the period from 1951 to 1961 showed that the incidence of syntropy was 2% of 451 pts. Distribution of pts. with syntropy was 7/120 with chronic lymphatic, 1/89 with chronic myeloid and 1/242 with acute leukemia. Of various interpretations given, none were endorsed or rejected.

- 64-364 RELATION OF BLOOD GROUPS A, B, AND O TO CARCINOMA OF THE STOMACH IN SAO PAULO.

(Por.) Branco Ribeiro, E. *An. Paul. Med. Cir.* 86(2):87-95, 1963.

A translation from the English of a paper abstracted as CRA 1(5):#979, 1963.

- 64-365 ARE CARCINOMAS OF THE BILIARY TRACT INCREASING? (Ger.) Nassr-Esfahani, H. (Dept. Surg., U. Göttingen, Germany) and P. E. Böhme. *Chirurg* 35(4):159-161, 1964.

Between 1951 and 1962, 653 biliary tract operations performed at the University of Göttingen included 45 carcinomas (6.9%). Division of this period into three 4-year intervals showed that the percentage incidence of carcinomas increased steadily from 4.8 to 10%. Female pts. were affected more frequently (68%) and at an earlier age than male pts.; in both sexes, no carcinomas were found before the age of 40 yr. This increase in the incidence of carcinomas of the extrahepatic biliary tract is attributed to a general increase in the rate of cholelithiasis after World War II. Since cholelithiasis is interpreted as a facultative precancerous condition, it is advocated that all gallstone pts. over 35 be subjected to surgery as an effective measure of cancer prophylaxis.

- 64-366 ETIOLOGIC AND PATHOGENIC PROBLEMS OF CANCER OF THE GALLBLADDER (A CLINICAL AND ANATOMOPATHOLOGIC CONTRIBUTION). (It.) Paliaga, A. (Inst. Clin. Surg., U. Rome). *Fegato* 7(4):382-394, 1961.

The literature related to the incidence of primary cancer of the gallbladder with respect to other localizations in the biliary ducts, in relation to sex, age, its geographic distribution, as well as possible etiologic factors is reviewed (32 references). Among 66 personal cases (25 operative and 41 diagnosed at autopsy) the male:female ratio was 1:10; the median age was 61.9 yr., with max. frequency between 50 and 70 yr. The author's findings confirm that cholelithiasis is a prominent etiologic factor. Calculosis was found in 94% of the cases and was often of long-standing duration in the history of the pt. Of 25 operative cases, 15/21 (14 females and 1 male) had presented calculi for more than 5 yr., 4/21 (2 females, 2 males) for 1-5 yr. and 6/25 (5 females, 1 male) for less than 1 yr. prior to hospitalization. Among other possible etiologic factors discussed were histologic changes induced by chronic cholecystitis (present in 80% of the author's cases), benign tumors of the gallbladder and embryonic inclusions.

- 64-367 OBSERVATIONS ON THE ETIOLOGY AND PATHOGENESIS OF CUTANEOUS EPITHELIOMA BASED ON THE STUDY OF 1519 TUMORS. (Fr.) Vilanova, X. (Dept. Derm. U. Barcelona, Spain) and L. A. Rueda. *Maroc. Med.* 43(464):7-17, 1964.

Among a total of 45,927 pts. with various dermatose

which were seen over a period of 15 yr. in the Department of Dermatology of the University of Barcelona, 1519 (3.3%) had cutaneous cancer; 98/1519 (65.1%) had basal cell carcinoma (BCC) and 521/1519 (34.9%) had spinocellular carcinoma (SCC). Among pts. with BCC, the sex ratio (male:female) was 409:589; at the time of tumor appearance, 29.2% were less than 50 yr. old and 8.8% more than 70 yr. old; in 97.2% the disease was localized to the head, in 2.3% to the trunk and in 0.3% to the extremities. Comparable figures for SCC were: 252:269, 13.2 and 37%; 88.4, 5.5, and 7.8%, resp. For BCC, distribution according to clinical type was "bead-like" forms, 60%; flat cicatricial types, 17.7%. Similarly for SCC: ulcerated forms 39.7%; button-shaped, 5.3%; vegetating, 21.3%. Sex bore no significant relationship to the clinical type of tumor. While tumors were mostly solitary, 5.3% of BCC and 4.2% of SCC were multiple forms. The frequency of BCC and SCC among the multiple forms was 48% and 29.3%, resp.; the remaining 22.67% had both tumors. A survey of various possible etiologic factors (including heredity, chemical compounds, chronic exposure to sunlight, precancerous lesions, trauma), which may have been involved in this series of pt. and a review of the literature relative to geographic distribution, race and environmental factors, showed that in the large majority of pts. with BCC etiologic factors were unknown or very difficult to establish and that in no case was the appearance of a BCC preceded by a known precancerous lesion; the consistent localization and the identical age of appearance of this tumor among different countries suggest that external factors are not involved in the development of BCC. In SCC on the contrary, etiologic factors can be almost always established and varies with the localization. Regardless of race or geographic distribution SCC arises on an altered skin, i.e., on a precancerous lesion which may be induced by radiations, chemical compounds, scars, burns, ulcers, fistulas, chronic granu-omas, and grafts.

368 PROPHYLAXIS OF CARCINOMA OF THE UTERINE CERVIX. (Sp.) Garcia, G., Pulido V., J. Bruguera, F. Alva, M. Villalobos, and J. C. de Laguna. *Ginec. Obstet. Mex.* (105):329-340, 1963.

An attempt to establish adequate prophylactic measures for carcinoma of the uterine cervix, the authors review (9 references) the results of previously published work investigating the importance of various factors (such as social, economic and environmental conditions, gynecologic and obstetric characteristics) which may be involved in its genesis. The early start of sexual relations and frequent deliveries (when compared to non-cancerous women) were common findings among women with cervical cancer while the number of abortions or pregnancies as such had no significance. The low incidence of cervical cancer

among women whose husbands were circumcised (Jews and Moslems) indicates that routine circumcision of all men is a desirable prophylactic measure. Data related to the frequency of carcinoma *in situ* were inconclusive as to its etiologic role. Among a total of 1784 gynecologic pts. seen at the Women's Hospital of Mexico from January 1961 to March 1963, 289 (16%) had cervical carcinoma; of these, 8% had carcinoma *in situ* and 5.8% microcarcinomas. The ratio of invasive carcinoma to carcinoma *in situ* was 10:0.9; in 1950-1951 the ratio was nearly the same, 10:0.5. Adequate treatment of carcinoma *in situ* is also recommended as an effective measure of preventing the development of invasive carcinoma.

64-369 A COMMENT ON THE PAPER "THE PROPHYLAXIS OF CANCER OF THE UTERINE CERVIX". (Sp.) Urrutia Ruiz, M. (General Hosp. Inst. Cancer, Mexico, D. F.). *Ginec. Obstet. Mex.* 18(105):340-342, 1963.

In a critical note on the paper of Garcia *et al.* (see previous abstract), the author states that in addition to the factors described there are several others of importance to be considered in the genesis of carcinoma of the uterine cervix; these included nutritional disorders, hormonal disturbances, cervical lesions (traumatic, infective, inflammatory) and benign lesions such as adenomas and polyps. The prophylactic measures advocated by Garcia are not sufficient in this author's opinion but should be supplemented by the improvement of nutritional, environmental, cultural and medical conditions of the lower classes and by the promotion of biannual medical examinations for women.

64-370 PREGNANCY AND CANCER. (Sp.) Zuckermann, C. *Tacitl* 4(1):3-6, 1964.

After discussing general figures as to the relationship of pregnancy with uterine, mammary and chorionic carcinoma and the frequency of the association of pregnancy and cancer, the author reports to have personally observed during 26 yr. of private practice the following cases of concomitant association of pregnancy with cancer: uterine cervix, 21 (invasive, 13; *in situ*, 8); breast, 8; skin, 4; chorionic endometrium, 6; chronic myeloid leukemia, 3; and 1 each rectum, vulva, bone, lymphoblastoma, Hodgkin's disease and melanoma.

64-371 MALIGNANT TUMOR MORTALITY IN VARIOUS COUNTRIES OF THE WORLD. (It.) Safier, M. *Ann. Sanit. Pubblica* 24(6):1013-1034, 1963.

A review of the standard figures of cancer mortality/100,000 people during the year 1958-1959 in 25 countries (for USSR data refer to 1960), including the incidence of mortality in relation

to site (esophagus, stomach, rectum, liver and biliary tract, lung, breast, uterus, prostate). Data are reported also for leukemia and aleukemic conditions.

- 64-372 THE CONTROL OF PRECANCEROUS CONDITIONS OF THE COLON AND RECTUM. (E.) Dukes, C. E. (Chester Beatty Res. Inst., Fulham Rd., London, S.W.3). *Canad. Med. Assn. J.* 90(10): 630-635, 1964.

The author reports on some pathological conditions which clinical experience has shown to be frequently followed by cancers. An important means of control of intestinal cancer is the early diagnosis and treatment of precancerous lesions. This precancerous tendency is relatively slight with solitary colo-rectal polyps, ulcerative colitis and bilharzial infestation, but it is exceptionally severe in familial colonic polyposis. At St. Mark's Hospital, London, England, for more than 30 yr., research on familial polyposis has been continued, and more than 90 families have been investigated and family pedigrees prepared. These now include 1050 "members", of whom 343 have had either polyposis or intestinal cancer, or both, the number with cancer being 243. Details of 3 affected families are given, with information on members of the third to fifth generations. As an example in family #1, after 38 yr. the third generation has 4 cases of polyposis all followed by cancer; in the 4th generation 3 cases of polyposis were seen, 2 of which have already been treated in the precancerous phase by operation.

- 64-373 PROBLEMS OF CARCINOGENESIS PRESENTED BY THE ASSOCIATION OF CANCER OF THE HYPOPHARYNX WITH CANCER OF THE URINARY SYSTEM. (Fr., Abstract of thesis) Jouvinroux, P. *Lyon Med.* 211(9):574-577, 1964.

In the conclusion of a graduation thesis discussing 5 observations of cancer of the hypopharynx associated with cancer of the urinary system, the author states that this association is most likely the product of simultaneous carcinogenesis induced by a carcinogenic compound and its metabolites.

- 64-374 FINAL RESULTS OF STATISTICAL STUDIES ON MORBIDITY OF LEUKEMIAS IN THE CRACOW DISTRICT IN THE YEARS 1951-1960. (Pol.) Janicki, K. (3rd Clin. Surg., Acad. Med., Cracow, Poland). *Pol. Arch. Med. Wewnet.* 34(2):139-146, 1964.

During the decade of 1951-1960, 2065 leukemia cases were hospitalized in the Cracow region; this constituted 35.3% of hospitalizations due to hematologic diseases in this region. Of these leukemia cases, 801/2065 who were registered for the first time served as the basis of this analysis. The regional incidence (801/2,331,058) was 3.4/10,000/10 yr. or 3.4/100,000/yr. A statistically significant increasing trend of incidence was established for this decade; this trend was particularly pronounced in yr. 1956-1958, with a marked decrease, however, in 1959, followed by an increase in 1960. The incidence (per 10,000 people/10 yr. period) was 0.6 for chronic granulocytic leukemia (CGL) and 1.0 for myeloblastic leukemia (ML), lymphatic leukemia (LL), or the group of unclassified leukemia (UCL); the increasing trend was greatest for ML, and insignificant for LL, UCL, and CGL (although the last showed an increasing trend which was close to the borderline of significance). Morbidity was significantly greater among men (4.3/10,000 men/10 yr.) than among women (2.7/10,000 women/10 yr.); the trend of increase in incidence was statistically significant for both sexes. Morbidity was significantly greater among city dwellers (4.1) than among country dwellers (3.1) with a statistically significant trend of increase among the country dwellers but not among city dwellers. Incidence of leukemia increased between the ages of 2-6 yr. (up to 7.5) and 55-75 yr. (up to 12.5); the av. incidence was 6.0 for those aged 45 yr. or more, 3.2 for children below 15, and 2.0 among those aged 15-44 yr. The tendency for increases in morbidity over the decade was statistically significant in all age groups; in children acute leukemia contributed most to this increase, whereas LL contributed most in adults. In comparison to av. morbidity in the whole of Poland, the morbidity for the Cracow region was lower in 1951-1955 and higher in 1956-1959. The increasing trend in leukemia incidence cannot be explained merely by improved diagnostic methods. (See also CRA 1(9-10):#1775, 1964.)

See also abstract nos.: 162, 165, 171

MISCELLANEOUS

- 64-375 CLINICAL AND MORPHOLOGICAL PARALLELS IN THE PRECANCEROUS AND NEOPLASTIC CONDITIONS OF THE UTERINE CERVIX. (Rus.) Krotova, L. I. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad). Vop. Onkol. 9(12):26-38, 1963.

Over 10,000 sections of uterine cervix from 80 uni- or multiparous pts. were studied. All pts. were subjected to hysterectomy for various conditions: fibromyoma with cervical ectropion but normal mucous membrane, 20/80; fibromyoma with hemorrhagic erosion and ectropion in 45/80; cervical squamous cell cancer (stage I) in 15/80. It was found that the degree of dystrophic changes in cervical tissues is closely related to changes occurring in cervical innervation. In cases of ectropion without erosions, the nerve elements showed symptoms of irritation and increasing reactive changes. In the precancerous stage, the changes were mostly of a reactive and proliferative nature. In squamous cell carcinoma all nerve elements showed manifestations of proliferation and destruction. The receptors were usually degenerated while the afferent fibers were totally disintegrated.

- 64-376 A PSYCHOPHYSIOLOGIC ANALYSIS OF CERTAIN FUNCTIONS OF HIGHER NERVOUS SYSTEM ACTIVITY IN INFANTS, CHILDREN AND EARLY ADOLESCENTS WITH LEUKEMOS AND OTHER MALIGNANT DISORDERS OF THE HEMATOPOIETIC, LYMPHATIC AND RETICULO-ENDOTHELIAL SYSTEM. (Ger.) Baltrusch, H.-J. F. (19 Babenend St., Oldenburg (Oldb.), Germany). Activ. Nerv. Sup. (Praha) 5(4):373-390, 1963.

Reported is an experimental psychological study of 60 pts. with leukemia and allied disorders, aged less than 1 to 14 (av., 6.7) yr. (36 boys and 24 girls). As to type, 40 had acute stem-cell, 2 had eosinophilic, 1 had chronic myeloid leukemia; 4 had leukemiform reticuloses; 2 had lymphosarcoma; 3 had reticulum cell sarcoma; and 5 had Hodgkin's disease. Three had leukemias (type not stated) associated with trisomal feeble-mindedness. Included in the evaluation procedures were both child and parent interviews, Rorschach's Test, the TAT, the CAT, the Machover technic, et al. The author concludes that children and early adolescents who develop leukemia or allied disorders have been exposed to a very much greater range and intensity of psychosocial stresses than normal children; and that the course of the disease is "directly dependent" upon the degree of continuing stress in the psychosocial environment. He states that emotional stress, negative emotions, and/or functional disturbance of nervous reflex activity weaken the organism's resistance in a non-specific way and initiate or foster development of the malignant process. (See also CRA 2(2):#165, 1964.)

- 64-377 THE INFLUENCE OF INTRAVASCULAR AGGREGATION ON THE SPREAD AND GROWTH OF

EXPERIMENTAL TUMORS. (E.) Gelin, L.-E. (Dept. Surg., U. Gothenburg, Sweden) and C.-M. Rudenstam. Bibl. Anat. (4):131-141, 1964.

In Sprague-Dawley rats inj. intraportally with 0.1 ml of methylcholanthrene-induced (MC) sarcoma cells and subjected to bilateral femoral fractures immediately after inj., hepatic and pulmonary metastases appeared within 2 wk. in 2/21 and 17/21 fractured animals, resp., and in 0/18 and 10/18 controls, resp. The number of pulmonary metastases per experimental animal was 3.0 (controls 1.7) and the number per animal with metastases was 3.7 (controls 3.0). In 2 groups of Sprague-Dawley rats inj. i.v. with Rous sarcoma (RS) cells (130,000) or MC sarcoma cells (120,000) followed by high molecular wt. Dextran (D; 2 g/kg i.v.) to induce intravascular aggregation, no difference in the frequency of tumor "takes" occurred in either group within 3 wk. compared to controls. Animals given RS cells had an av. of 6.6 metastases (controls, 4.0) as compared to an av. of 35 metastases (controls, 21) in animals given MC sarcoma cells; the number of metastases/animal with tumor "take" was 8.7 and 52, resp. (controls 5.7 and 26). In Sprague-Dawley rats given 40,000 RS cells into a mesenteric vein 1 day after D (2 g/kg into tail vein), the number of animals with hepatic metastases, the av. number of metastases/animal and the number of metastases/animal with "take" was 28/41 (controls, 23/40), 29 (controls, 10) and 40.9 (controls, 18.3), resp.

- 64-378 DEVELOPMENT OF A MENINGIOMA AROUND A FOREIGN BODY. (Ger.) Schmidt, H. (Dept. Surg., U. Kiel, Germany) and G.-H. Jaquet. Zbl. Neurochir. 24(2/3):65-73, 1963.

Forty yr. after a darning needle was thrust into the skull of an infant boy (apparently during the first few mo. of life, in an attempt at infanticide), the bearer died of a meningioma which had developed around the part of the foreign body which lay within the middle cranial fossa.

- 64-379 DEOXYRIBONUCLEIC ACID, RIBONUCLEIC ACID AND PROTEIN IN EXPERIMENTAL TISSUE REGENERATION AND CARCINOGENESIS. (Ger.) Büchner, F. (Inst. Pathol., U. Freiburg, Germany), W. Oehlert and H. Noltenius. Deutsch. Med. Wschr. 88(47):2277-2283, 1963.

In a review of previously published experimental studies, supplemented by report of a study of rats undergoing unilateral nephrectomy + a single i.p. inj. of 0.2 ml 1% soln. of mercuric chloride, the authors conclude that the transformation of normal parenchymal cells into malignant cells is a gradual process involving progressive changes in DNA. Only those cells are involved which have maintained or recovered their capacity for DNA synthesis. In experimental carcinogenesis, the latency time can be shortened significantly if

the rate of DNA synthesis can be increased. Experimental carcinogenic activity is not only a function of total dosage, in the sense of a simple sum of individual doses, but also a function of elapsed time by itself. (See also CRA 1(9-10):#1718 and *ibid.*, #1822, 1964.)

- 64-380 THE ASSOCIATION OF GASTRIC EPITHELIAL HYPERPLASIA AND CANCER. (E.) Monroe, L. S. (Scripps Clin. Res. Found., La Jolla, Cal.), G. A. Boughton and S. C. Sommers. *Gastroenterology* 46(3):267-272, 1964.

The extent and type of gastric epithelial hyperplasia (EH), classified as foveolar, glandular or combined (foveolar and glandular) according to the region of the gastric mucosa involved, in 100 pts. with stomach cancer was 45%, 5% and 41%, resp. Among 100 controls, EH involvement in 92 pts. with duodenal ulcer was 18%, 4% and 3%, resp. While the remaining controls, 8 gastric pts., were too few for statistical significance, the av. EH involvement was 17%, 15% and 8% and fell between values for the cancer and duodenal ulcer pts. In the 100 cancer pts., 59 were 100% involved with EH, while 5 pts. showed a complete absence of EH involvement; of the 100 controls, none were 100% involved with EH, while 26 showed a complete absence of involvement with EH. Four unsuspected cancers (2 adenocarcinomas, 2 lymphomas of the stomach) were found in the gastric ulcer pts.; of the cancer pts. 19 showed carcinoma *in situ* around the margin of invasive primary lesions and 10 of these pts. showed total EH involvement. No hyperplastic pyloric glands were found in the cancer pts.

- 64-381 CHROMOSOME CHANGES IN HUMAN LEUKEMIA AND A TENTATIVE ASSESSMENT OF THEIR SIGNIFICANCE. (E.) Nowell, P. C. (Dept. Path., U. Pennsylvania Sch. Med., Philadelphia) and D. A. Hungerford. *Ann. N.Y. Acad. Sci.* 113 (Art.2):654-662, 1964.

After reviewing (27 references) previous reports on chromosome 21 aberrations found in chronic granulocytic leukemia, myeloproliferative disorders, acute leukemia (adults and children), chronic lymphocytic leukemia and miscellaneous disorders the authors stress the need for careful examination of poor as well as good metaphases from pts. with leukemia in view of the fact that phytohemagglutinin-free cultures frequently give few and technically poor mitotic figures. Childhood leukemia associated with Down's syndrome revealed, besides the expected 21 trisomy, an atypical chromosome 21 also found in the subject's mother and presumably unrelated to the disease. One case of acute monocytic leukemia presented an extra, small, acrocentric (group 21-22) chromosome whose presence was most likely due, however, to extensive X-ray therapy. In studies of Waldenström's macroglobulinemia, 6 cells from peripheral

blood cultures revealed larger acentric fragments possibly derived from an additional large chromosome.

- 64-382 CHROMOSOMAL DIFFERENCES AMONG THE ACUTE LEUKEMIAS. (E.) Sandberg, A. A. (Roswell Park Memorial Inst., Buffalo, N. Y.), T. Ishihara, Y. Kikuchi and L. H. Crosswhite. *Ann. N.Y. Acad. Sci.* 113(2):663-716, 1964.

The karyotypes of bone marrow cells were examined in 75 pts. with acute myeloblastic (34 pts.) or lymphoblastic (41 pts.) leukemia, the majority of whom had received chemotherapeutic agents (such as busulfan, 6-mercaptopurine, methylglyoxal-bis-guanyldrazone, vincristine, chlorambucil, cyclophosphamide, methotrexate, leurocristine, urethan, or hydroxyurea) previously or during various stages of the disease. For identification of homologous chromosomes, the Denver number system was combined with Patau's alphabetical grouping. Aneuploidy in the pts. with acute lymphoblastic leukemia was invariably hyperdiploid and included 5 pts. with a mode of 92 or more chromosomes and these pts. seemed to respond more readily to chemotherapy; their lymphoblasts had an unusual appearance in the marrow smears. Group C9 was the most commonly involved, by having extra autosomes, followed by group G; abnormalities of the A1 chromosomes occurred in 4 pts. and abnormal marker chromosomes were found in 5 pts. In the pts. with acute myeloblastic leukemia, aneuploidy was hypodiploid (as low as 41) with groups C and G again being involved either by having missing or extra autosomes; marker chromosomes were present in 4 pts. Of these pts., 5/34 who were elderly had a bimodal cell population and slightly hyperdiploid modes (47-48) which were characterized by instability of the chromosome constitution. In 40/75 pts., the modes appeared diploid. The authors note that the data do not lend themselves, at present, to an interpretation of the relation of chromosomal changes to the causality of acute leukemia, but the findings may be of considerable diagnostic and therapeutic help.

- 64-383 CHROMOSOMAL CHANGES IN HUMAN LEUKEMIA. I. CHRONIC MYELOID LEUKEMIA. (Rus.) Tsearskaia, T. P. (Clin. Hematol., Centl. Inst. Hematol. Blood Transfus., Moscow), G. V. Osechenskaia and S. A. Khrustalev. *Probl. Gemat.* 9(1):3-10, 1964.

In a study of 339 bone marrow cells from 6 pts. with chronic myeloid leukemia, chromosome distribution was as follows: 43-45 in 8; 46 in 310; 47-48 in 12; 87 and over in 9. One pt. had 47 chromosomes in 15% of the cells. The Philadelphia chromosome was seen in all pts. and was present in an av. of 82% of the cells (56-93%). Treatment with cytostatics (busulfan or 6-mercaptopurine) tended to reduce the number of Philadelphia chromosomes; this decrease was also seen in pts. with a long duration of disease.

- 64-384 CHROMOSOME STUDIES IN LEUKEMIA. I. EVIDENCE FOR THE ORIGIN OF LEUKEMIC STEM LINES FROM ANEUPLOID MUTANTS. (E.) Reisman, L. E. (Child Res. Ctr. Michigan, Detroit), M. Mitani and W. W. Zuelzer. New Eng. J. Med. 270(12):591-597, 1964.

Chromosome studies were performed on bone marrow and peripheral blood preparations from 52 children with leukemia (42 "stem cell" or lymphatic, 4 granulocytic, 1 monocytic, 2 atypical, 2 chronic myelogenous and 1 chronic monomyelogenous); also studied were 20 pts. with other hematologic disorders as well as normal controls. Aneuploidy with chromosomal modes varying from case to case (47-65) was consistently found in the active stages of leukemia, both in initial pretreatment phases and in relapse, mo. or yr. after the onset. During remissions induced by various chemotherapeutic agents (prednisone, 6-mercaptopurine, methotrexate, busulfan, cyclophosphamide), the normal diploid mode of 46 chromosomes was restored irrespective of the duration or type of therapy. Controls showed normal diploid chromosomes. In the 2 pts. with chronic granulocytic leukemia, the degree of suppression of the leukemic stem line during or after adequate busulfan therapy did not appear to be as thorough as that achieved with the chemotherapeutic agents in the acute leukemias; the pseudodiploid cells with the unique marker of chronic leukemia always remained demonstrable in large numbers during remission. An additional 5 cases studied in successive relapse, remission and relapse phases have all shown recurrence of the original aneuploid stem lines. (See also CRA 1(9-10):#1825, 1964.)

- 64-385 ASSOCIATION OF MALIGNANT TUMOR AND COLLAGEN DISEASE. (Jap.) Nagahara, S. Dept. Path., Shinshu U. Sch. Med., Japan) and T. Shirasawa. Sogo Rinsho (Clin. All-round) 3(1):158-163, 1964.

Three autopsy cases are presented of association of malignant tumors (2 carcinoma of the stomach, 1 sympathicoblastoma of the adrenal gland) and collagen disease (2 dermatomyositis, 1 periarthritis nodosa). In one pt. there was believed to be an allergy due to oncocytemia in the sympathicoblastoma which was combined with a change of the tumor cells by X-irradiation which caused the periarthritis nodosa. In another pt. the dermatomyositis was believed to be related to an allergy associated with tuberculosis and to metastases of the tumor to the muscle. No causative factors were noted between the tumor and the collagen disease in the third pt.

- 64-386 PRICKLE CELL CARCINOMA ON THE SO-CALLED KRAUROSIS VULVAE (REPORT OF TWO CASES). (Jap.) Kobayashi, T. (Dept. Derm., Chiba U. Sch. Med., Japan) and I. Takeuchi. Hifu To Hinyo Derm. Urol. 25(6):694-698, 1963.

Microscopic studies are reported of 2 cases of prickle cell carcinoma which developed from Kraurosis vulvae. (1) A 62-year-old Oriental female experienced itching over the external genitalia 2 yr. prior to development of tumor over the area. Biopsy 3 yr. after start of first symptoms established the diagnosis of prickle cell carcinoma. (2) An 80-year-old Oriental female had leukorrhea 3 mo. before diagnosis of prickle cell carcinoma. No etiologic factors were described in either case.

- 64-387 TRAUMA AND CARCINOGENESIS IN THE AREAS OF THE MOUTH, NASAL SINUSES, AND EAR. (Ger.) Wirth, G. (Clin. Ear Nose Throat, U. Heidelberg, Germany). HNO 11(12):347-349, 1963.

Three cases are presented where insurance claims had arisen from presumed connections between trauma and tumor development. In case 1, a squamous carcinoma of the tongue was found 5 mo. after severe and therapy-resistant injury to the tongue; a causal relationship was considered likely. In case 2, a meningioma invading the ethmoidal mucosa was not considered related to burns of the face suffered 8 yr. earlier. In case 3, carcinomatous degeneration of a perichondritis of the ear 8 wk. after accidental trauma was considered highly unlikely.

- 64-388 MALIGNANT LYMPHOMAS IN THE HARE AND CAT. (Fr.) Nicod, J.-L. (Inst. Path. Anat., Lausanne, Switzerland) and H. Burgisser. Path. Microbiol. 27(1):1-7, 1964.

In addition to one previously described in the hare, the authors report a case of Brill-Symmers disease in a female cat of unknown age. Also observed were a neoplasm corresponding closely to Hodgkin's disease in man which was found in a female hare, and two cases of reticulum cell sarcoma which had developed in adult hares (one female, one male).

- 64-389 ORIGIN OF CANCER. (PART III) GRAPHS OF A FEW OF THE PHYSICAL, CHEMICAL AND BIOLOGICAL PROPERTIES OF CANCEROUS CELLS. (Sp.) Uribe Valdes, G. (Natl. U. Mexico, Mexico City). Medicina (Mex.) 44(932):38-42, 1964.

According to the author, cancer originates following an anaphylactic shock at the cellular level which will induce the following sequence of events: fragmentation of the protoplasmic proteins with the increase of the number of the protoplasmic molecules and therefore of the intraprotoplasmic osmotic pressure; the latter change will produce an inflow of the extracellular fluid with the increase of the protoplasmic mass; the protoplasm/nucleus mass ratio will therefore be altered and this change will result in changes of the internal pressures in the nucleus, bringing about a karyokinesis and a subsequent cellular division.

The greater the protoplasmic mass and the protein alterations, the higher will be the frequency of cell division.

- 64-390 THE DNA CONTENT OF CARCINOMA IN SITU. (Ger.) Kother, L. (Inst. Path., U. Giessen, Germany) and W. Sandritter. Gynaecologia 157(1):9-19, 1964.

Cytophotometric studies on 2 specimens of carcinoma in situ of the cervix showed an atypical distribution pattern of DNA, with a base line showing hypotetraploid and/or triploid values. Measurements in 3 different cell layers (basal, middle, and upper layer) of one of the tumors confirmed the morphological impression of absence of differentiation: all layers consisted of cells having the same abnormal DNA distribution pattern characteristic of chromosomal aneuploidy. It was therefore concluded that carcinoma in situ is a true preinvasive carcinoma.

- 64-391 GIANT-CELL XANTHOFIBROMA OF THE TIBIO-TARSAL JOINT. (It.) Giambelli, G. (Clin. Orthoped., U. Milan, Italy) and G. Questa. Gazz. Int. Med. Chir. 68(24):2814-2823, 1963.

Reported is the case of a 25-year-old man who developed a giant cell xanthofibroma of the tibiotarsal joint 3 yr. after a severe sprain of the same articulation. After reviewing controversial interpretations of the etiology and pathogenesis of this condition, the authors conclude that in this case trauma may have been a determining factor in the appearance of the tumor.

- 64-392 THE NATURE OF KERATOACANTHOMA AND ITS PLACE AMONG CUTANEOUS EPITHELIAL TUMORS. (Fr.) Nicolau, S. G. (Min. Health and Prev. Med., Bucharest, Rumania) and L. Băluș. Oncologia (Basel) 17(2):120-134, 1964.

After discussing the histopathologic and clinical characteristics of keratoacanthoma as well as the favorable course of this condition (which in the majority of the cases regresses and disappears spontaneously after a few mo.), the authors report a rare observation of malignant transformation of this tumor in a 72-year-old woman. After surgical excision of the initial tumor, which was localized in the right supraorbital region, followed by diathermocoagulation, the pt. developed 2 local recurrences in 7 mo. The first

recurrence, larger than the initial tumor, had still the clinical and histologic aspects of a keratoacanthoma (although cellular proliferative activities appeared to be increased) and was treated with extensive and deep diathermocoagulation. The clinical aspect of the second recurrence (developed 4 mo. after the previous one) was that of an ulcerated epithelioma and biopsy disclosed carcinomatous degeneration.

- 64-393 BENIGN AND MALIGNANT CONDITIONS. (Sp.) Hamperl, H. (Inst. Anat. Path., U. Bonn, Germany). Arch. Fac. Med. Zaragoza 11(6): 801-809, 1963.

In a general discussion of the diagnostic problems encountered by the pathologist in everyday practice, with special reference to cancer of uterine cervix and the sequence of gradual morphologic changes which go before, it is concluded that a definite separation between benign and malignant characteristics does not exist. The author also attempted to establish the existence of benign and malignant types of gastric lymphoreticulosarcoma in relation to the subsequent favorable or unfavorable course of the condition but failed to show any correlation.

- 64-394 REACTION BETWEEN NORMAL AND LEUKAEMIC CELLS IN VITRO. (E.) Pegrum, G. D. (Dept. Hemat., Charing Cross Hosp. Sch. Med., London, W.C.2). Nature (London) 201:1139-1140, 1964.

Mixed peripheral leukocyte cultures were prepared using WBC from a female pt. with chronic myeloid leukemia plus a karyotype showing the presence of a Ph¹ chromosome and WBC from a normal male with a standard karyotype. The WBC were adjusted to 10,000; 0.5 ml aliquots from each were mixed and incub. for 48 hr. at 37°C with nutrient medium TC 199. Colcemid was added at 44 hr.; after 4 hr. the cells were exposed to hypotonic soln., fixed with ethanol-acetic acid and stained with orcein acetic. With normal WBC alone there were no divisions. Leukemic cells showed occasional divisions while in the mixed cultures there were many mitoses. The chromosomes of the mixed cells were all female, some showing the Ph¹ character. In the leukemic cells there were 17% large "blast type" cells with 2.2% in metaphase; in the mixed cultures counts were 35% and 5.3%, resp. These results suggest a possible antigenic reaction between leukemic cells and normal WBC.

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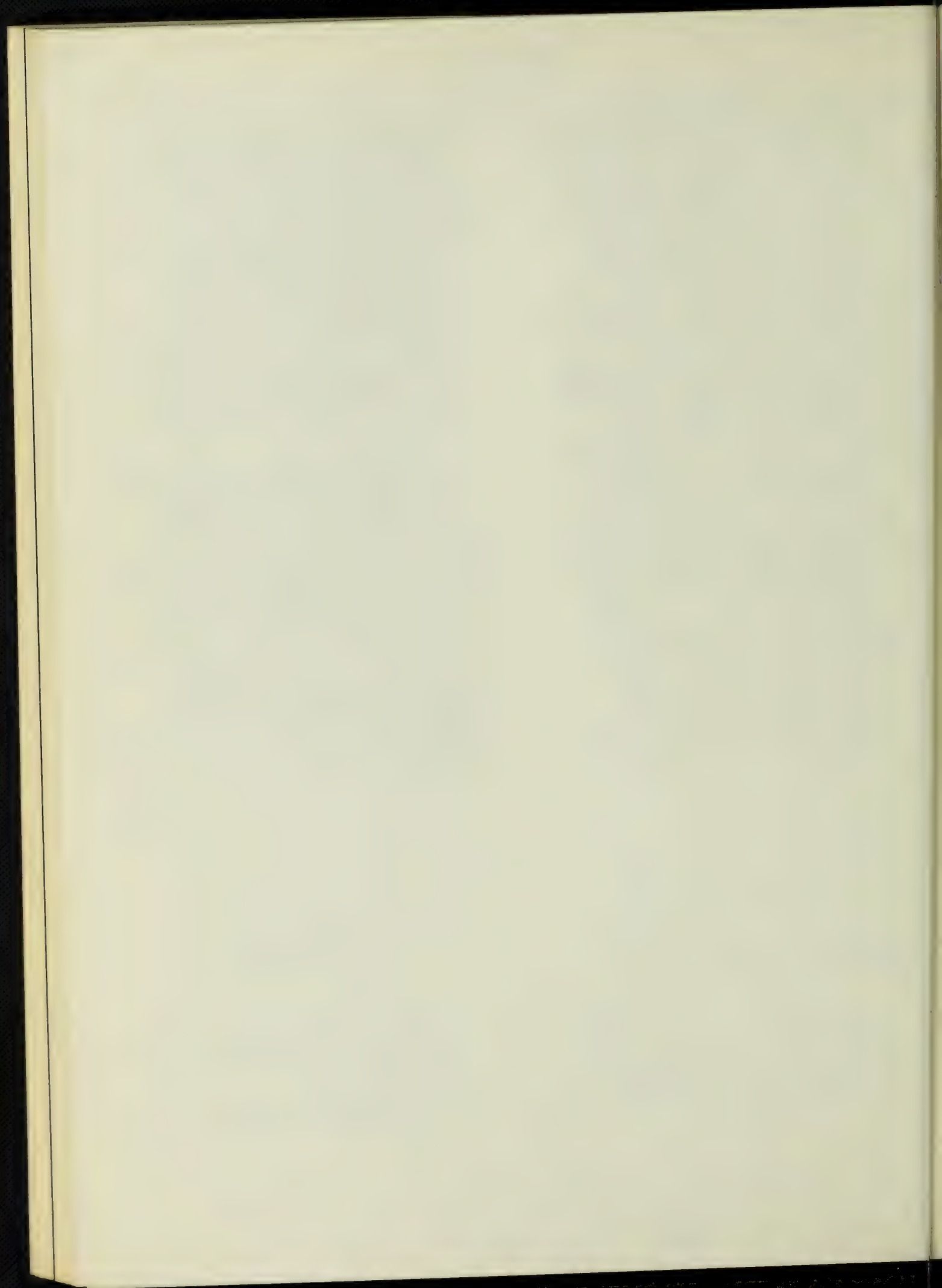
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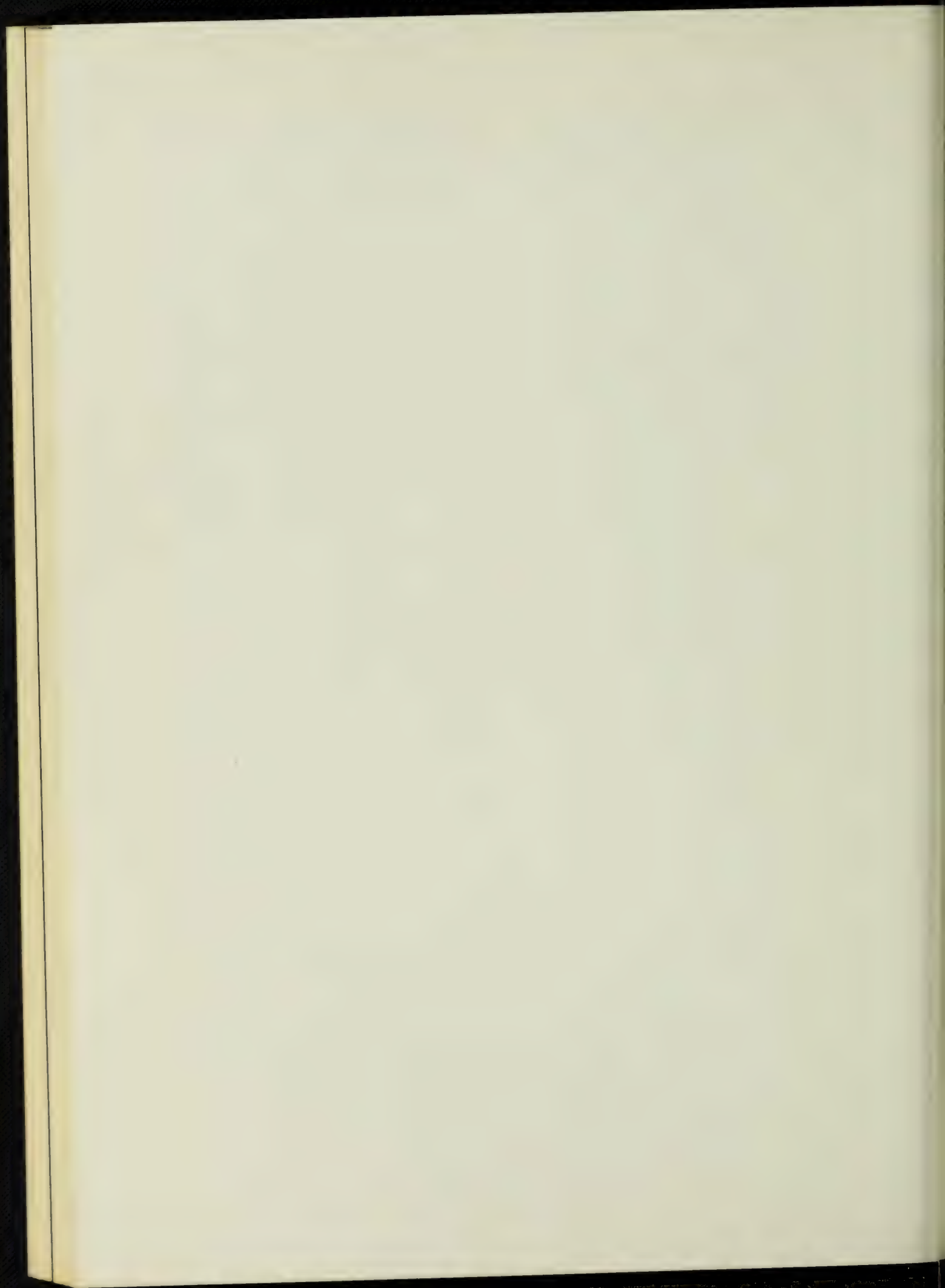
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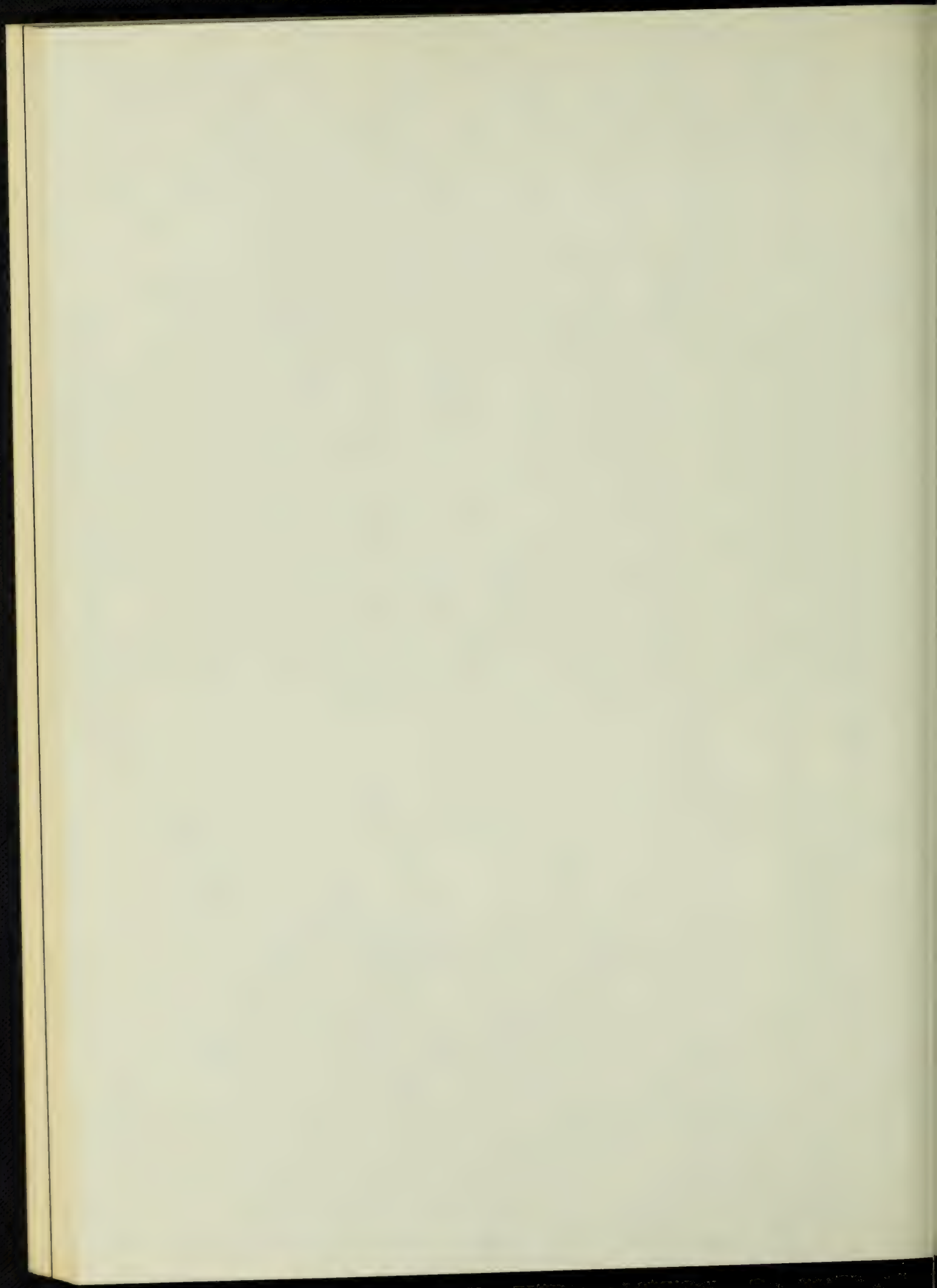
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CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS

ABSTRACTS

Volume 2, Number 3
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubate(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	lc.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

4-395 SOME REMARKS CONCERNING THE CONTRIBUTION OF R. F. A. ALTMAN, "THE ORIGIN OF THE FIRST CANCER CELL". (Ger.) Schmidt, F. (German Acad. Sci., Berlin). Arch. Geschwulstforsch. 19(2):144-149, 1964.

The author defends various theories of carcinogenesis attacked by Altman (report published in Arch. Geschwulstforsch. 19(1,2):97, 1962) such as the virus etiology, the mutation theory, and Schmidt's own "cancer induction theory". He then enumerates various arguments against Altman's hypothesis that malignant degeneration of a cell starts at the cell membrane, and that carcinogens act as "lipophilic sensitizers" which eventually provoke unlimited cellular proliferation. He concedes, however, that problems of permeability and surface phenomena may be of greater significance than has been recognized in the genesis, growth and therapy of cancer. (45 references)

4-396 THE SEPARATION AND ANALYSIS OF POLY-NUCLEAR AROMATIC HYDROCARBONS PRESENT IN THE HUMAN ENVIRONMENT. I. (E.) Sawicki, E. Robert A. Taft Sanitary Engin. Ctr., Cincinnati, Ohio). Chem. Anal. 53(1):24-30, 1964.

After presentation of a list of carcinogenic hydrocarbons and where they occur there is a discussion of methods of their separation by sublimation and vacuum distillation. Presented in some detail are methods of separation by solid-liquid extraction, liquid-liquid extraction and column chromatography. (See also CRA 1(12):#2095, 1964.) (127 references)

4-397 CURRENT KNOWLEDGE AND THEORETICAL CONCEPTS OF THE ETIOLOGY AND PATHOGENESIS OF MALIGNANT TUMORS. (Ger.) Döntenwill, W. (Inst. Path., U. Munich, Germany). Med. Klin. 58(48):1949-1952, 1963.

Concepts of carcinogenesis currently discussed in the literature are reviewed. From the etiological point of view, the following possibilities are discussed: (1) Exogenous carcinogens, such as hydrocarbons, ionizing radiation, viruses, etc., (2) Endogenous carcinogens, such as sterins, steroids, etc., (3) Cocarcinogenic factors promoting proliferation, (4) Genetically determined disposition. (47 references)

4-398 A REVIEW OF THEORIES OF CARCINOGENESIS. (Ger.) Graffi, A. (German Acad. Sci., Berlin). Arch. Geschwulstforsch. 22(1-2):13-41, 1964.

In a review of current theories of carcinogenesis, the author concludes that enough is now known concerning the role of nucleic acids in relation to intracellular genetic changes to reconcile the

"mutational" and "viral" schools of thought via development of a single, common concept. It is doubtful whether there is a specific, single explanation of carcinogenic change inasmuch as the development of the autonomous state, on the part of a single cell, can probably come about in response to a number of processes or situations capable of creating genetic changes at different genetic loci. Thus this phenomenon, like the carcinogenic stimulus as such, is probably heterogeneous in nature as concerns both the initiation of the process and the finer mechanisms involved in its subsequent development. (177 references)

64-399 THE SIGNIFICANCE OF THE INTRACELLULAR NUCLEIC ACID METABOLISM AND THE HOST CELL-VIRUS RELATIONSHIP FOR VIRUS INFECTIONS. (E.) Leuchtenberger, C. (Dept. Cytochem., Romand Anticancer Res. Inst., Lausanne, Switzerland). Bibl. Microbiol. 22(4):18-42, 1964.

An extensive review and discussion of the author's previous studies (see CRA 1(4):#593; ibid., (5):#838, 1963 and ibid., (9-10):#1644, 1964) on intracellular nucleic acid metabolism and the host cell-virus relationship in virus infections. (29 references)

64-400 CELL-VIRUS RELATIONSHIPS WITH TUMOUR VIRUSES. (E.) Stoker, M. (Inst. Virol., U. Glasgow, Scotland). Brit. Med. Bull. 20(2):145-148, 1964.

After a brief discussion of the characteristics of tumor viruses, the author describes the transformation effect of Rous virus on tumor cells, as well as the inability of Rous virus to multiply without the addition of a "helper" virus. Cell-virus relationships with DNA tumor viruses, such as polyoma virus (see CRA 1(3):#468 and ibid., (5):#790, 1963), rabbit papilloma virus and SV40 virus, are also studied. (34 references)

64-401 THE AROMATIC AMINES. (E.) Clayson, D. B. (Dept. Exptl. Path., U. Leeds, England). Brit. Med. Bull. 20(2):115-120, 1964.

See CRA 1(9-10):#1636, 1964. In addition, bladder tumors due to tryptophan metabolites and tissue reactions of the aromatic amines are also discussed. (63 references)

64-402 III. SHORT-TERM AND LONG-TERM EFFECTS. B. THE LONG TIME EFFECTS OF NUCLEAR WAR. (E.) Newell, R. R. (Stanford U. Sch. Med., Palo Alto, Cal.). Conn. Med. 28(3):207-211, 1964.

The author reviews the commonly recognized late sequelae of radioactive fallout, such as leukemia, cancer, shortening of the lifespan and genetic

mutations. Mutagenesis is particularly studied in regard to genetic effects of large radiation doses, recessive mutations, homozygosity, heterozygosity and combined radiation effects. (5 references)

- 64-403 CANCER INDUCTION BY NATURAL PRODUCTS.
(Ger.) Schmäh, D. Deutsch. Med. Wschr. 89(12):575-576, 1964.

The author points out that carcinogenicity is not confined to by-products of our technological age, but is also inherent in many natural products. As an example, he mentions the betel nut, which appears to be responsible for the high incidence of cancer of the oral cavity in certain Asiatic countries (35x higher incidence than in Europe); the carcinogenic principle is believed to become active only when the nut is chewed together with tobacco leaves. Other examples are the Senecio alkaloids (isatin, isatidin and retrorsine as liver carcinogens in rats), and the nitrosamine-like constituents of the cycad nut; the latter 2 plants may play a role in the frequent occurrence of primary liver carcinoma in Africa and Guam. Tannic acid and certain constituents of peanut meal have also been shown to induce liver carcinoma. (9 references)

- 64-404 ANTIVIRAL CHEMOTHERAPY AS A BASIS FOR CHEMOTHERAPY OF MALIGNANT BLOOD DISEASES AND NEOPLASMS. (It.) Magrassi, F. (Inst. Special Path. Med., Naples, Italy). Riforma Med. 78(9):225-231, 1964.

After discussing several unsuccessful *in vivo* and *in vitro* attempts to destroy the pathogenic properties of leukemogenic (Friend, Rauscher) and tumorigenic (polyoma) viruses with xenamine or xenaldial, the author reviews the results of researches aimed at the discovery of biochemical alterations which may arise in the host during the various phases of the viral infection. In the case of Friend's virus induced leukemia, it has been demonstrated that coincident with the transformation from the infective stage to the initial phase of leukemia glycolysis and protein synthesis are increased in the host spleen while tryptophan pyrrolase activity of the liver is decreased. The importance of studies of this type is stressed particularly in relation to the discovery of metabolic alterations responsible for the leukemic transformation of the viral infection as well as a source of information in the search of drugs which might interfere with these metabolic changes and therefore prevent such a transformation. (20 references)

- 64-405 GASTRIC CARCINOMA AND SMOKED FOODS.
(E.) Schmäh, D. (Inst. Path., U. Bonn-Venusberg, Germany). German Med. Monthly 9(2):78, 1964.

Essentially the same as the review abstracted as CRA 1(11):#1855, 1964. (11 references)

- 64-406 IMMUNOFLUORESCENCE OF ONCOGENIC VIRUSES.
(Ger.) Löffler, H. (Inst. Hyg., U. Basel, Switzerland). Bull. Schweiz. Akad. Med. Wiss. 20(1):48-53, 1964.

Reports on the demonstration of viruses by means of the fluorescent antibody technic are reviewed. The method is suitable for the localization of oncogenic as well as non-oncogenic viruses, as long as the virus material is antigenic, i.e., protein in nature; this condition is fulfilled more often *in vitro* than *in vivo*. In tumors due to DNA viruses, such as the Shope papilloma virus in wild rabbits, a virus-specific fluorescence is found in the nuclei of cells in the keratohyaline layers; it is found less often in the superficial, completely cornified layers, and never in the deeper, proliferating layers of cells. Also in the tissues infected with polyoma virus, fluorescing viruses were demonstrable in the already clearly damaged cell layers, but not in the actively proliferating parts of the tumor. Although virus multiplication accompanied by cell destruction appeared to precede cellular proliferation taking place in the absence of demonstrable virus multiplication, it was not clear whether the first phenomenon led to the other or was an essentially independent aspect of virus infection. In the extra-nuclear RNA virus infections, virus-producing and "malignant" cells are at least partly identical. Since both can be found in the early stages of polyoma virus infections, there seems to be no major difference between "infectious, necrotizing" viruses and "oncogenic" viruses. (34 references)

- 64-407 ON THE EXPERIMENTAL INDUCTION OF CARCINOMA OF THE ESOPHAGUS. (Ger.) Gibel, W. (Robert-Rössle-Clin., German Acad. Sci., Berlin-Buch) and G. Wittig. Deutsch. Gesundh. 19(14):635-637, 1964.

After a short review of substances commonly known to produce malignancies of the upper alimentary tract (coal tar, naphthylamine, azo dyes, urethan, methylcholanthrene, dimethylbenzanthracene, benzpyrene, and P32), it is pointed out that nitrosamine, and related heterocyclic N-nitroso derivatives, especially dinitrosopiperazine, methyl-nitrosourethan, nitrososarcosine ethylester, and ethylvinyl nitrosamine, are local carcinogens, producing (in the rat) carcinomas of the pharynx, tongue, or esophagus, and that i.v. admin. of nitrosopiperazine has also induced esophageal carcinomas, thus showing a true organotropic action. The possibility is suggested that the carcinogenic activity of tobacco may be due partly to the formation of these compounds through burning of N-containing substances during smoking, or to biosynthesis of carcinogenic diazo-alkanes from nitrosamines by intracellular enzymatic oxidation. The

Authors also suggest that alcohol plays a cocarcinogenic role in relation to tobacco in inducing human esophageal carcinoma. (13 references)

- 408 CHARACTERISTICS OF CARCINOGENESIS IN MUSCLES WITH VARYING METABOLISM. (E.) Erdnyakov, O. M. Bull. Exp. Biol. Med. 55(2):1-190, 1964.

Translation from the Russian of a paper which appeared in Biull. Eksp. Biol. Med. 55(2):78-83, 1963 and abstracted as CRA 1(2):#213, 1963. (13 references)

- 409 THE PROBLEM OF INHIBITORY FACTORS IN AZO DYE CARCINOGENESIS IN THE LIVER. (Sp.) Baba, T. (Nat'l. Res. Inst. Cancer Ctr., Tokyo). Nippon Rinsho (Jap. J. Clin. Med.) 11(1):2393-2396, 1963.

This review deals with several subjects: (1) inhibiting factors in azo dye carcinogenesis (one of which is p-hydroxypropiophenone); (2) the relation of sex to azo dye carcinogenesis; (3) histochemical distribution of protein bound azo dye studied with C^{14} -dimethylaminoazobenzene. (13 references)

- 410 A CHILDREN'S CANCER DEPENDENT UPON ENVIRONMENT. (Sp.) Burkitt, D. (Dept. Surg., Makerere U. Coll. Sch. Med., Kampala, Uganda, Africa). Acta Oncol. 2(1):16-25, 1963.

Description of a lymphoma syndrome observed in Southern Africa, including material previously reported in CRA 1(3):#467, 1963 and ibid., 1(12):1-7, 1964. (13 references)

- 411 A CLIMATIC DEPENDENT CHILDREN'S CANCER. (E.) Burkitt, D. (Dept. Surg., Makerere U. Coll. Sch. Med., Kampala, Uganda, Africa). Ethiopian Med. J. 1(5):254-258, 1963.

CRA 2(1):#410, 1964. (8 references)

- 412 THE ACQUIRED IMMUNOLOGICAL TOLERANCE OF THE TURKEY TO ROUS SARCOMA VIRUS. (E.) Harris, R. J. C. Acta Oncol. 2(1):43-50, 1963.

Review including material previously reported in CRA 1(3):#461, 1963. (18 references)

- 413 LIVER TUMORS INDUCED BY RADIATIONS. (Fr.) Lacassagne, A. (Curie Found., Paris). Rev. Franc. Etud. Clin. Biol. 9(3):1-272, 1964.

Author reviews the literature regarding hepatic tumor formation following treatment with radium, thorium, Au¹⁹⁸ and total X-irradiation.

A comparative review of personal studies on liver changes after partial X-irradiation and admin. of various chemical carcinogens, such as dimethylaminoazobenzene (see CRA 1(11):#1898, 1964), carbon tetrachloride, 2-acetylaminofluorene, dimethylnitrosamine, follows. Fibrotic transformation of connective and vascular tissue of the liver, leading to cirrhosis, was found to be common to both surface irradiation and implantation of radioelements in hepatic parenchyma. (21 references)

- 64-414 THE GROUP OF PAPOVA VIRUSES, AND IN PARTICULAR SIMIAN VIRUS SV40. (Sp.) Melnick, J. L. (Dept. Virol. Epidemiol., Baylor U. Coll. Med., Houston, Texas). Acta Oncol. 2(1):51-62, 1963.

A short review of the literature, including material previously abstracted in CRA 1(5):#945, 1963; and ibid., 1(12):#2142, 1964. (24 references)

- 64-415 THEORETICAL EVALUATION OF TAUTOMERIC TRANSFORMATIONS WITH NUCLEIC ACIDS AND THEIR ROLE IN MUTATIONS. (Rus.) Sukhorukov, B. I. (Inst. Phys. Chem., Acad. Sci. USSR, Moscow) and V. I. Poltev. Biofizika 9(2):148-159, 1964.

A review of the literature on theoretical consideration of tautomerism of nucleic acids is presented. Schematic drawings, equations and tables on dissociation constants of various ribosides of nucleic acids, xanthine and its N-methyl derivatives, and the nitrogenous bases are included. The role of tautomerism in cellular mutations is discussed. (24 references)

- 64-416 THE MOUSE LEUKEMIA VIRUS (GROSS). (Sp.) Gross, L. (Cancer Res. Unit, VA Hosp. Bronx, New York). Acta Oncol. 2(1):37-42, 1963.

A short review including material abstracted previously in CRA 1(1):#100; and ibid., (4):#721, 1963. (21 references)

- 64-417 BIOLOGICAL AND PATHOLOGIC PROPERTIES OF SIMIAN VIRUS 40. (Sp.) Eddy, B. E. (NIH, Bethesda). Acta Oncol. 2(1):26-36, 1963.

A review of the literature, including results previously reported in CRA 1(6):#1121, 1963; ibid., (11):#1843; and ibid., 2(1):#81, 1964. (62 references)

- 64-418 HORMONAL FACTORS IN CHEMICAL CARCINOGENESIS. (E.) Bielschowsky, F. Ann. Fac. Med. Perugia 53(4):369-376, 1963.

In this address the author reviews the literature on chemical carcinogenesis and discusses his recent work showing the influence of pituitary

factors on hepatoma development in mice and rats. With pituitary dwarf mice, hepatoma formation caused by aminofluorene (AF) was delayed but not completely blocked. These experimental animals also differed in their response to DMBA applied to the skin: there was less gross damage and papillomas appeared later and in fewer numbers. Even when a promotor, croton oil, was applied this reduced susceptibility to DMBA was obvious. Admin. of a thyroid supplement to these animals enhanced growth, sexual development and hepatoma formation. Hypophysectomized rats, on the contrary, showed marked reduction in hepatoma formation after treatment with AF, with no effect noticed upon addition of thyroid supplement. A discussion of the nature of this protective pituitary factor follows. (20 references)

- 64-419 EFFECTS INCLUDING CARCINOGENESIS OF ^{131}I AND X-RAYS IN THE THYROID OF EXPERIMENTAL ANIMALS: A REVIEW. (E.) Doniach, I. (London Hosp., London E.1). Health Phys. 9(12): 1357-1362, 1963.

After a discussion of the effects on thyroid function of ^{131}I and X-rays, the author considers the carcinogenic action of the two agents and compares them quantitatively (1,000 rad X-rays = quantitative effect of 10,000 rad ^{131}I). The increased sensitivity of the thyroid to external X-irradiation is also discussed. (32 references)

- 64-420 OUTLINES OF THE PATHOPHYSIOLOGY AND ETIOLOGY OF LEUKEMIAS. (Rus.) Bernar, G. Probl. Genet. 8(12):3-12, 1963.

A Russian translation of a paper presented at

the 9th International Hematological Congress in Mexico, in 1962, consisting mainly of a review of the literature on the course, etiology, mortality and epidemiology of leukemias. (46 references)

- 64-421 ENDOGENOUS DEFENSE AGAINST MALIGNANT TUMORS. (Ger.) Wilken, H. (Women's Clin., U. Rostock, Germany). Zschr. Aerztl. Fortbild. (Jena) 58(5):253-258, 1964.

Current concepts of cancer immunology are reviewed. Endogenous defenses such as the properdin system, non-specific resistance to malignancies, and specific antibody formation against tumor antigens are discussed. Utilization of these mechanisms in tumor diagnosis and immunotherapy is outlined. (No references)

- 64-422 CHROMOSOMAL ABNORMALITIES IN HEMOBLASTOSES. (Ger.) Remy, D. (Dept. Med., Municipal Hosp., Bremen, Germany). Deutsch. Med. Wschr. 89(14):684-688, 1964.

Numerical and structural chromosomal aberrations reported in the literature in connection with acute and chronic leukemias, lymphosarcoma, Hodgkin's and Waldenström's disease, and plasmacytoma are reviewed. The only specific aberration demonstrated to date is the occurrence of the Philadelphia chromosome in chronic myeloid leukemia, while reports of other aberrations associated with chronic lymphatic leukemia and other hemoblastoses are isolated and conflicting. In acute leukemia, multiple--mostly aneuploid--aberrations were found, but there was no consistency; similar changes were observed in mongolism associated with acute leukemia. (62 references)

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estimated as 7 pC (approx. 20 mrem/yr.) and 5 mrem/yr., resp. Increments should be added in 1963 of 25 mrem for Sr⁸⁹ and of 10 mrem for external radiation. Forecasts for 1964 suggest that doses should be of the same order as for 1963 but should "decrease thereafter".

- 64-428 THE EFFECT OF IONIZING RADIATION ON MITOSIS IN MALIGNANT AND BENIGN EPIDERMAL HYPERPLASIA IN THE MOUSE. VI. EFFECT OF A SINGLE CONTACT IRRADIATION AFTER 60 DAYS OF PRETREATMENT WITH A CARCINOGEN OR TUMOR INITIATOR. (Ger.) Setälä, K. (Inst. Path. Anat., U. Helsinki, Finland), B. Lindroos and O. Nyyssönen. *Strahlentherapie* 123(1):99-124, 1964.

Groups of 80 female RA mice received local application to the skin of the back of either, 9,10-dimethyl-1,2-benzanthracene (DMBA; 60 µg) or Tween 60 (97 mg) for 60 days. On day 61 the treated skin of some mice in each series was exposed to one treatment of 1000 rad/9 min. of Sr⁹⁰ + Y⁹⁰ contact irradiation. When studied at periods of 1, 6, 12, 24, 48 and 72 hr. after irradiation, it was found that the malignant, DMBA-induced hyperplasia was considerably more sensitive to radiation than the benign, Tween 60-induced hyperplasia. The DMBA-treated tissue showed a higher incidence of degenerating nuclei, and a significantly greater number of mitotic aberrations, in spite of the fact that the rate of mitosis prior to irradiation was significantly lower.

- 64-429 TUMOR PRODUCTION IN RATS OF VARIOUS AGES BY MEANS OF WHOLE BODY X-IRRADIATION. (Ger., Abstract) Stutz. *Med. Welt* 64(1):65, 1964.

Whole body X-irradiation (270 r) of rats of various ages (5 days before birth and 13, 49 and 121 days after birth) showed that females developed more tumors than males, mostly benign genital tumors. Their formation presupposes an intact female endocrine system. Age at time of irradiation had no bearing on the number of tumors, i.e., there was no increased sensitivity to radiations in fetal or early life.

- 64-430 DENTURE CARCINOMA OF THE HARD PALATE. PROBLEMS AND TREATMENT. (Ger.) Salis-Samaden, R. von (Centl. Radiol. Inst., State Hosp., Salzburg, Austria). *Radiol. Austria*. 14(3):191-195, 1963.

The etiological role of chronic mechanical irritation due to dentures in the development of malignancies of the palate is discussed. It is a rarity, accounting for not more than 1-2% of mouth or jaw carcinomas. The author reports 6 cases; 3/6 were verified histologically as squamous cell carcinomas, while in 3/6 there were

mucosal changes showing some evidence of malignant degeneration. The patients (2 males, 4 females; ranging in age from 33 to 65 years) had worn dentures with or without suction cups for 2-14 yr. In 3/6, the changes affected the medial raphe, which the author considers the favored site of this type of tumor. All were treated with radioactive strontium contact irradiation, 12,000-15,000, resp., and were cured within less than 2 mo.

- 64-431 TUMOR DEVELOPMENT IN THE RAT BY BLOOD PLASMA ULTRAFILTRATE FROM IRRADIATED ANIMALS. (E., Abstract) Souto, J. (Agric. Res. Lab., U. Tennessee-Atomic Energy Comm., Oak Ridge). *Radiat. Res.* 22(1):239, 1964.

In experiments involving 2,145 Sprague-Dawley rats, males and intact and ovariectomized females, certain conclusions can be made. There is a significant increase of mammary tumors in female rats when plasma or plasma ultrafiltrate from irradiated rat or sheep is inj. at 7 days of age or within 24 hr. of birth. There were no changes in tumor incidence when female rats were inj. at 6 mo. of age.

- 64-432 INFLUENCE OF SEX, ENVIRONMENT, AND RADIATION FACTORS ON LIFE SHORTENING AND TUMOR INCIDENCE IN C3Hf MICE. (E., Abstract) Grahn, D. (Div. Biol. Med. Res., Argonne Natl. Lab., Ill.) and K. F. Hamilton. *Radiat. Res.* 22(1):191, 1964.

When 100-day-old C3Hf/He mice of both sexes were studied by comparing life-span data derived from small cages (19.6 inches²) of 3 mice versus 1 mouse at 2.6 r/day of gamma radiation and control, results indicated statistically significant radiation and cage effects, along with small sex effect, on mean after survival. In contrast, hepatoma incidence responded to cage environment and sex but not to radiation. Female hepatoma incidence rose from 13% for singles to 39% for trios, while in males it only rose from 53% to 67%. Ovarian tumor incidence responded to radiation but not significantly to caging.

- 64-433 NEOPLASMS IN MICE PRODUCED BY PARTIAL-BODY EXPOSURE TO X-RAYS. (E., Abstract) Finkel, M. P. (Argonne Natl. Lab., Ill.), B. O. Biskis and P. B. Jenkins. *Radiat. Res.* 22(1):188, 1964.

Mortality and gross pathology data 650 days after exposure of the hind legs and adjacent tissues of 1800 CF1 female mice showed that survival was the same for exposure levels of 250, 625 and 1,000 r of X-rays and that tumors were induced in both bone and soft tissues. The incidence of osteogenic sarcomas in the irradiated area after exposures of 250, 625 and 1,000 r was 1.9, 6.0 (the calculated incidence at 625 r was 6.3%) and 10.7%, resp. Incidence of soft-tissue tumors in the

irradiated area for the above exposure levels was 4.1, 5.1 and 5.0%, resp. Incidence in the same area among suitable control mice was 0.1%.

64-434 SKIN TUMOR INDUCTION IN THE RAT BY UNIFORM AND GRID PATTERN BETA RADIATION. (E., Abstract) Albert, R. (Dept. Indust. Med., New York U. Med. Ctr., N. Y.) and F. Burns. Radiat. Res. 22(1):166, 1964.

Acute skin damage and tumor incidence in rats were measured following single exposures to yttrium⁹¹ beta radiation applied either uniformly to a 25-cm² area or in parallel stripes, 1 mm wide and 2 or 5 mm apart. Surface doses ranged from 2,760-12,700 rads for uniform and from 4,200-15,050 for the grid radiation. Even at 15,000 rads, the acute ulceration from grid radiation was found to be negligible; in contrast, substantial ulceration occurred with uniform radiation at 4,200 rads. The close agreement between predicted and observed incidence in the grid radiations suggests that tumor formation is proportional to the amount of irradiated skin.

64-435 MYELOGENOUS LEUKEMIA AND ACUTE RETICULOSIS IN BEAGLES AFTER Sr⁹⁰ ADMINISTRATION. (E., Abstract) Biskis, B. O. (Argonne Natl. Lab., Ill.), M. P. Finkel and I. L. Greco. Radiat. Res. 22(1):169-170, 1964.

Osteosarcomas appeared in great numbers, but no leukemia was found, among 45 dogs (beagle) following treatment with 150 µC/kg of Sr⁹⁰ in one inj. or in daily inj. throughout 1 yr. On the contrary, no osteosarcomas were seen in 39 dogs receiving 15 µC/kg in 278 divided inj., but 1/39 has died of chronic myeloid leukemia and 1/39 of acute reticulosis.

64-436 CHRONIC TOXICITY OF INHALED PLUTONIUM IN DOGS. (E., Abstract) Park, J. F. (Biol. Lab., Hanford Lab., GE Co., Richland, Wash.), W. J. Bair and W. J. Clarke. Radiat. Res. 22(1):222-223, 1964.

Single 10-30 min. exposures of 40 beagles to plutonium (Pu²³⁹O₂) aerosol resulted, after 28-48 mo., in the death of 7/40 dogs after deposition of 4-9 µC in the lungs. The body burden at death was 1.5-3 µC with about 50% localized in the lungs, up to 50% in the bronchial and mediastinal lymph nodes of some dogs, 2-10% in the liver and 1-4% in the skeleton. Av. radiation dose to the lungs was 9,000-23,000 rads. After 36 mo., 4/40 dogs revealed bronchiolo-alveolar tumors, in addition to severe fibrotic and metaplastic changes. Most of these neoplasms were locally invasive and of multicentric origin, and no evidence of regional or distant metastasis was seen.

64-437 POLONIUM-210 IN LUNGS AND SOFT TISSUES OF CIGARETTE SMOKERS. (E., Abstract)

Little, J. B. (Dept. Physiol., Harvard Sch. Publ. Health, Boston, Mass.), E. P. Radford, Jr., H. L. McCombs, V. R. Hun and C. Nelson. Radiat. Res. 22(1):209, 1964.

Polonium-210 (Po²¹⁰) levels in peribronchial lymph nodes in 5 non-smokers and 12 chronic smokers who smoked until 1-10 days prior to death were similar, av. 0.011 pC/g wet tissue (range: 0.006-0.020). Po²¹⁰ in lung parenchyma showed considerable variation within the same lung, while the av. level in smokers (0.008 pC/g; range: 0.002-0.020) was 4 times that of non-smokers (0.0018 pC/g; range: 0.001-0.002). In the bronchial epithelium of proven non-smokers little or no Po²¹⁰ has thus far been found; in smokers, however, the av. levels per g of tissue were 4-40 x greater than in smoker's parenchyma. Except for pulmonary tissue, no differences were seen in Po²¹⁰ levels of smokers and non-smokers, although urinary excretion of Po²¹⁰ is higher in smokers. (See also CRA 2(2): #195, 1964.)

64-438 COINCIDENCE OF LEUKEMIA WITH PRIMARY MULTIPLE SKIN CARCINOMAS. (Cz.) Vilček, E. (Dept. Radiol., Comenius U. Bratislava, Czech.). Cesk. Radiol. 18(1):54-58, 1964.

A 47-year-old man developed a total of 62 skin tumors within a period of 15 yr. (initially, spinocellular, then basal cell carcinoma predominated); he was treated with local irradiation. Within 14 yr. of this period, general weakness, fatigue, anorexia, loss of wt., and general pains developed, and chronic myeloid leukemia was diagnosed. It was concluded that the ionizing radiation therapy admin. for 11 yr. prior to development of leukemia (total 272,500 r) may have had a leukemogenic effect in this case.

64-439 THOROTRASTOMA OF THE CUBITAL FOSSA WITH NECROSIS AND EARLY MALIGNANT GROWTH. (Cz.) Kolář, J. (Clin. Radiol. Fac. Gen. Med., Charles U., Prague, Czech.), R. Vrabec and Z. Král. Cesk. Rentgen. 17(5):334-337, 1963.

After a review of incidence of granulomas and malignant degenerations after diagnostic admin. of radioactive contrast isotopes (19 references), a case report is presented. A woman (age 54) was hospitalized 27 yr. previously for jaundice and inj. probably with Thorotrast i.v., but part of it was extravasated into the cubital fossa resulting in painful induration which persisted but became painless in a few mo. The pt. presented with local necrosis and calcifications evident in X-ray. Typical deposits in spleen and hepatic lymph nodes confirmed that the agent used 27 yr. previously was Thorotrast. The necrotic area was excised and histologically early malignant degeneration was noted (degenerative changes included cellular and nuclear paratypia of epithelial cells and striking irregularities of fibrocytes and histiocytes).

- 64-440 IN VIVO MEASUREMENT OF THOROTRAST IN LIVER AND SPLEEN BY GAMMA SPECTROMETRIC ANALYSIS. (E., Abstract) Cohn, S. H. (Med. Res. Ctr., Brookhaven Natl. Lab., Upton, L. I., N. Y.), E. A. Gusmano, S. W. Lippincott and J. S. Robertson. Radiat. Res. 22(1):177, 1964.

A technic for the determination of the body burden of Thorotrast ($\text{Th}^{232}\text{O}_2$) is described. The problem was amenable to soln. by application of spectrometric analysis of gamma-ray emitting daughters of Th^{232} such as Tl^{208} , Ac^{228} , Bi^{212} , and Pb^{212} .

- 64-441 THE DEVELOPMENT OF LEUKEMIA IN LETHALLY IRRADIATED MICE PROTECTED WITH CELLS FROM MICE OF A HIGH INCIDENCE LEUKEMIA STRAIN. (E.) Hays, E. F. (Dept. Biophys. Nucl. Med., U. California Sch. Med., Los Angeles) and E. M. White. Blood 23(5):557-563, 1964.

A more detailed presentation, with larger numbers of experimental animals, of the paper abstracted as CRA 1(6):#1039, 1963.

- 64-442 PROGRESS REPORT: PLUTONIUM REMOVAL, TUMOR INCIDENCE STUDIES. IV. (E.) Rosenthal, M. W., J. F. Markley and A. Lindenbaum. Pp. 87-91 in Argonne National Laboratory. Biol. Med. Res. Div., Semiannual Report, July-Dec., 1962. ANL-6790. Biol. and Med. (TID-4500, 27th Ed.). U. Chicago, Ill. Contr. W-31-109-Eng.-38. Off. Tech. Ser., Dept. Comm., Washington, D. C., 236 pp., \$3.00, 1963.

CF#1/An1 75-day-old female mice were inj. i.v. with monomeric plutonium (Pu^{239} ; 2.7 $\mu\text{C/kg}$ in 0.30 ml) followed 1 hr. or 3 days later by 500 mg/kg of diethylenetriaminepentaacetic acid (DTPA; 500 mg/kg/day x 12 i.p.); DTPA was given alone to another group of animals. At the time of the report, only a preliminary survey of bone tumor incidence following admin. of monomeric Pu can be made since many mice were still alive. When a comparison was made between mice treated with monomeric and polymeric Pu (2.6 $\mu\text{C/kg}$), followed by DTPA 3 days later (controls given saline instead), the latent period of bone tumor induction was 236 days (controls, 153 days) and 325 days (controls, 269 days), resp., while the tumor incidence at death from the end of the latent period to 400 days was 67% (controls, 81%) and 25% (controls, 56%); the 400 day survival was 65% (controls, 28%) and 65% (controls, 54%), resp. At 400 days, mice treated with monomeric Pu, followed by DTPA 1 hr. later had about the same survival (85%) as that of the control group receiving only DTPA (90%) and the latent period was longer and the tumor incidence was lower; i.e., the only mouse with a possible bone tumor died at day 354. Distribution and excretion studies were also performed.

- 64-443 MEDICAL RADIATIONS AND LEUKAEMIA: A RETROSPECTIVE SURVEY. (E.) Gunz, F. W.

(Christchurch Hosp., Christchurch, New Zealand) and H. R. Atkinson. Brit. Med. J. 1:389-393, 1964.

The histories of exposure to medical radiations were obtained from 590 pts. with leukemia (355 acute, 78 chronic granulocytic, 157 chronic lymphocytic) and 122 pts. with myelomatosis (712 controls); the leukemia pts. consisted of 87.3% of all leukemias known to have occurred in New Zealand between March 1958 and December 1961. In the acute and chronic granulocytic leukemia pts., a significant excess (2.86%) of therapeutic irradiation was seen as compared to the pts. with myelomatosis and the controls and this was restricted to pts. who had received relatively large doses (integral doses above 1.5 mega-g r or bone marrow doses above 10 r), while lower doses were equally common in pts. and controls; the excess became more striking when the pts. who had therapy more than 15 yr. before disease onset were excluded. In the pts. with chronic lymphocytic leukemia who had high dose radiotherapy, 17.2% had a complicating relationship between the leukemia and the cancers for which the irradiation was given and therefore, it is possible that the leukemia may have arisen from a genetic predisposition rather than as a result of radiotherapy. Bone-marrow doses due to diagnostic radiation were low (av. 1.31-2.04 r) and in the 10 yr. prior to disease onset, 49% of the pts. with acute leukemia, 72.9% with chronic granulocytic leukemia, 62.3% with chronic lymphocytic leukemia, 55.8% with myelomatosis and 61.2% of the controls had diagnostic radiation. Individual pts. may have had high doses but it is thought unlikely that more than 1% of the acute and chronic granulocytic leukemias were due to diagnostic radiation exposure. Intra-uterine diagnostic irradiation was given during pregnancy to the mothers of 13.7% of the leukemic children as compared to 12.3% of the mothers of the controls.

- 64-444 A STUDY OF TUMOR TYPES PRODUCED BY ULTRA-VIOLET LIGHT IN HAIRLESS AND HAIRY MICE. (E.) Epstein, J. H. (Dept. Med., U. California Sch. Med., San Francisco) and W. L. Epstein. J. Invest. Derm. 41(6):463-473, 1963.

The posterior backs of brown hairless inbred mice, (21) were irradiated with UV (15.34×10^7 ergs/cm²; 280-320 m μ) over a 7-mo. period. During a period up to 60 wk. there developed 18/21 squamous cell carcinoma, 1/21 fibrosarcoma, 0/21 melanotic tumor, and 2/21 benign tumor. In Group II 22 hairless mice were irradiated with the same UV dosage which was preceded by a single application to the back of 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.1 ml, 0.5% soln.); tumors induced were, resp., 18/22, 0/22, 2/22 and 2/22. Group 3 consisted of 13 inbred Swiss mice with tumors induced on the back by the same dose of DMBA but was followed by chronic low dosage of UV (13.33×10^7 ergs/cm²), an amount considered cocarcinogenic but not carcinogenic under the conditions of study. Tumors induced were, resp., 6/13, 4/13, 0/13 and 3/13. Prior application of DMBA in Group II led to

markedly shortened latent period and more rapidly growing, more frankly malignant tumors with more metastases. In Group III the squamous cell carcinomas were poorly differentiated and did not appear to metastasize; fibroplasia was more prominent. In Group II 12 hairless mice developed blue papules; 2 of these became large melanotic tumors after prolonged UV irradiation.

64-445 STUDIES ON RF MOUSE LEUKEMIA INDUCED BY X-RAY IRRADIATION. IV. CELL-FREE TRANSMISSION. (Jap., Abstract) Sota, S. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino and K. Ikejiri. Nippon Ketsueki Gakkai Zasshi (Acta Hemat. Jap.) 26(3,4):390, 1963.

See CRA 2(2):#206, 1964.

64-446 CARCINOMA OF THE MAXILLARY SINUS FOLLOWING THOROTRAST INSTILLATION. A FURTHER REPORT. (E.) Buda, J. A. (Coll. Phys. Surg., Columbia U., New York), J. J. Conley and R. Rankow. Am. J. Surg. 106(5):868-871, 1963.

Three pts. (2 males, 46 and 49; 1 female, 70 yr.) with past history (15-20 yr. previously) of roentgenographic studies of the sinuses with Thorotrast, complained of a draining fistula (2 pts.) and continual nasal discharge. Roentgenograms and biopsies led to the diagnosis of squamous cell epithelioma of the right maxillary sinus in all 3 cases, of which one was later reclassified as carcinoma (muco-epidermoid type). Right radical maxillectomy was performed in all cases; all the specimens showed radioactivity consistent with that of thorium and its decay products.

64-447 CONTRIBUTION TO THE ORIGIN OF MALIGNANT TUMORS AFTER THOROTRAST. (Ger.) Freese, P. (Inst. Path., Acad. Med., Magdeburg, Germany) and P. Kemnitz. Zbl. Allg. Path. 105(3/4):161-169, 1964.

Three pts., aged 42-69 yr., developed malignant tumors 23-29 yr. after admin. of Thorotrast (T). In 1/3, a squamous cell carcinoma of the kidney with hepatic, pulmonary, and skeletal metastases was found 27 yr. after presumed retrograde pyelography with T. In 1/3, malignant hemangioendothelioma of the liver developed 24 yr. after cephalo-arteriography with T; and in 1/3, a primary liver carcinoma was detected 29 yr. after cephalo-angiography. The T dosage was not known. In all cases, at autopsy the agent was demonstrated histochemically in the malignant

tumors as well as in the RES and in the vicinity of the inj. site, where characteristic tissue changes were found.

64-448 INTRAVENOUS INJECTION OF GUERIN EPITHELIOMA HOMOGENATES. I. IN THE RAT AFTER X-IRRADIATION. (Fr.) Driessens, J. (Inst. Cancer Res., Lille, France), A. Clay, J. Vanlerenberghe, G. Giaux, L. Adenis and P. Quandalle. C. R. Soc. Biol. 157(11):1981-1983, 1963.

The deep irradiation (400 r) of Wistar rats (strain Gif) of both sexes, av. wt. of 200 g, 1 mo. prior to the i.v. inoc. of Guerin epithelioma homogenate resulted in the development of metastases in 31/58 animals (lymph nodes, 27; lungs, 21; adrenals, 10; kidney, 8; liver, 1) and quiescent conc. of malignant cells in 4/58 (lungs). Metastases were found only in 12 of 56 non-irradiated rats. (See also CRA 1(9-10):#1803; and ibid., (11):#2038, 1964.)

64-449 TESTING OF MEMBRANE FILTERS FOR CARCINOGENIC EFFECTS IN RATS. (Ger.) Teichmann, B. (Robert-Rössle-Clin. Acad. Sci. Berlin, Berlin-Buch). Naturwissenschaften 51(6):143-144, 1964.

Membrane filters made of regenerated cellulose or cellulose esters have been used in experimental implantation of diffusion chambers into rats and surgically treated cancer pts. Such filters were found devoid of carcinogenic activity when implanted into Wistar rats. The circular filters of 14 mm diameter, varying in thickness from 80 to 120 μ , were implanted i.p., s.c. or intracutaneously (10 rats per group). After 370 and 455 days, resp., the tissue surrounding the implants was not pathologically altered.

64-450 TWO CASES OF CARCINOMA OF THE LOWER LIP AFTER CRYOTHERAPY. (Ger.) Profirov, D. (Clin. Dermatol. Vener. Dis., U. Plovdiv, Bulgaria). Derm. Wschr. 149(13):330-331, 1964.

Squamous cell epithelioma of the lower lip developed 5 mo. and 1 yr., resp., after dry ice treatment of a cheilitis glandularis apostematosa and a lupus erythematosus. In both cases, a "syncarcinogenic" mechanism was assumed, since several potential carcinogens (chronic inflammation, sunlight, atrophic scars, smoking, and cryotherapy) had acted simultaneously or in succession. The dry ice treatment was considered to have triggered the eventual malignant degeneration.

See also abstract nos.: 402,413,419,475,508,562

CHEMICAL CARCINOGENESIS

64-451 EXPERIMENTAL ANALYSIS OF THE FACTORS CONTROLLING THE PROLIFERATION OF EPITHELIUM AND OF MALIGNANT EPITHELIAL TUMORS IN TRITURUS. (Ger.) Seilern-Aspang, F. (Austrian Inst. Cancer Res., Vienna) and K. Kratochwil. Arch. Geschwulstforsch. 21(2):113-137, 1964.

In a study of possible cell regulatory mechanisms in the epithelium of the newt, the responsiveness of cells was eliminated by s.c. inj. or topical application of carcinogens (dibenzanthracene, benzpyrene), or by placing the animals in a saturated aqueous soln. of Tween 60. The latter method produced epithelial hyperplasia in the survivors, while the former induced tumors with a tendency toward invasive growth and metastatic dissemination, but also toward spontaneous regression via differentiation. When intertissual control was eliminated by infliction of wounds at various levels, it was found that the regenerating epithelium did not become hyperplastic when in contact with the basal membrane or the outer layer of the s.c. connective tissue, but did become so when, due to the depth of the inflicted wound, it was in direct contact with the pigmented cell layer, the partially destroyed connective tissue, or the muscle tissue. These hyperplasias were arrested by accumulation of embryonic connective tissue cells in the wound area. By i.p. inj. of methylene blue or India ink, this cell accumulation was prevented, and the hyperplastic epithelium grew invasively into the connective tissue and muscle layers. Hyperplasia was also produced by subepithelial implantation of cellophane or connective tissue. The higher control functions were eliminated by impairment of the viability of the animals through i.p. inj. of non-carcinogenic hydrocarbons or methylene blue or by hypophysectomy; each of these methods produced epithelial hyperplasia.

64-452 CHROMOSOME CHARACTERISTICS OF THREE TRANSPLANTABLE RAT LEUKEMIAS. (Rus.) Fichidzhian, B. S. (Lab. Cytogen., Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and E. E. Pogosiants. Vop. Onkol. 9(12):47-51, 1963.

The chromosome complements of 3 transplantable rat leukemias (Strains L-37, L-26 and ILK) derived from DMBA-induced spleen and liver neoplasms were studied. All 3 leukemias are superdiploid and showed limited variation in chromosome number. L-37 has 44 chromosomes and 2 additional elements, one metacentric and one telocentric. L-26 has 45 chromosomes and one additional element within each morphological type (meta-, telo-, and subtelocentric). ILK also has 45 chromosomes and 2 markers: micro and small telocentric, resp.; ILK also showed trisomy of the largest telocentric chromosomes. The cytogenetic individuality of these leukemias has not changed during many (up to 20) transplant generations.

64-453 TRANSPLANTABLE CARCINOMA OF RAT KIDNEY (STRAIN RA). (Rus.) Ākimova, R. N. (Ukrainian Res. Inst. Exptl. Clin. Oncol., Kiev, USSR). Vop. Onkol. 9(12):51-55, 1963.

Kidney tumors and cysts developed after prolonged feeding of castrated rats with 6-methylthiouracil; after s.c. transplantation of one of these tumors a rat kidney adenocarcinoma (Strain RA) was obtained. After s.c. and intratesticular inoc. tumor takes were 98% and 100%, resp. Tumors appeared 4-6 days after inoc. of 0.3-0.5 ml of tumor suspension into 2-6-month-old rats of both sexes. The s.c. induced tumors were tuberous, fleshy neoplasm with a solid consistency; metastases were absent. Twenty-five-30 days after intratesticular inoc. large metastases were found in the greater and lesser omentum, intestinal mesentery and diaphragm, but rarely in the spleen. In later generations this tumor achieved a solid constitution without indication of the glandular structure which was found in the first 4 generations. Up to the present time 33 generations have been obtained with both inoc. Average survival times were, after s.c. inoc. 25-27 days, and after intratesticular inoc. 25-33 days. No spontaneous regression of tumor was observed.

64-454 INCIDENCE OF SQUAMOUS CELL CARCINOMA IN MICE FED 9,10-DIMETHYLBENZ(a)ANTHRACENE. (E.) Mulay, A. S. (NCI, Bethesda). Nature (London) 200(Suppl.):1114-1115, 1963.

When 9,10-dimethylbenz(a)anthracene (DMBA; 30 mg% emulsion in 5% Triton 100, 0.3 ml intragastric) was admin. to 2 or 6-month-old C57Br and C3H male and female mice, the incidence of squamous cell carcinoma of the forestomach was 73.5% in C57Br mice (3 feedings/wk. x 10 to a total of 2.7 mg) after 245 days, 40.5% in C3H mice (2 feedings/wk. x 4, followed by 1 feeding/wk. x 7 to a total of 1.35 mg) after 245 days and 8.5% in C57Br mice (90 µg in a single feeding) after 300 days; no appreciable sex difference in the tumor incidence was seen, except the 4 carcinomas in the third group all occurred in females. One squamous cell carcinoma of the forestomach was seen in 1/23 C57Br female controls treated with 0.05% Triton 100 in drinking water but no carcinoma occurred in 10 male controls and another group of 51 male and female controls. Hyperkeratosis of the forestomach was seen in the controls and the DMBA-treated mice. Mice treated with a single dose of DMBA showed 3 (6.4%) precancerous lesions and 14 (29.8%) papillomas, while all the mice in both control groups showed no precancerous lesions but 5.9% had papillomas.

64-455 THE CARCINOGENIC PROPERTIES OF CHOLESTEROL AND ITS 5 AND 7 HYDROPEROXIDES. (Ger.) Koch, R. (Radiol Inst., U. Freiburg i. Br.,

Germany). *Arzneimittelforschung* 15(12):1116-1117, 1963.

See CRA 1(5):#889, 1963.

64-456 INDUCTION OF NEOPLASMS WITH 2-ACETYL-AMINOFLUORENE. (Pol.) Górski, T. (Dept. Neoplastic Biol., Inst. Oncol., Gliwice, Poland). *Nowotwory* 13(4):297-302, 1963.

2-Acetylaminofluorene (AAF) was fed at a conc. of 0.05% in the diet for 2-12 mo. to 26 rats (8-11 mo. at start) and 15 mice (3 mo.). Among 20 rats which survived 8-12 mo. there developed 4 cholangiomas, 2 mammary cancers, 2 hepatomas and 3 hemangiomas. Six rats died of lung infection after 7-8 mo. Only 6/15 mice survived beyond 7 mo. of AAF feeding. When sacrificed after 12 mo. one hepatoma was observed. The author discusses the role of experimental conditions (age, sex, diet and strain of animals) in AAF-induced carcinogenesis.

64-457 EXPERIMENTAL STUDIES OF METAPLASIA OF THE UTERINE MUCOSA IN MICE. (Pol.) Górski, T. (Dept. Neoplastic Biol., Inst. Oncol., Gliwice, Poland) and A. Draszcz. *Pat. Pol.* 14(4):439-447, 1963.

Methylcholanthrene (M; 0.1-2 mg in olive oil) was instilled into the ligated uterine horns of 2-4-month old R_{III}, BN or A mice. In order to potentiate any metaplasia-inducing effect of M, the R_{III} mice also received estrogen (100 U x 2/wk. s.c.) or cortisone (0.25 mg x 2/wk. s.c.). Controls received only estrogen or cortisone. After 3 wk.-6 mo. of treatment no metaplasia of the isolated uterine horns was found. Hyperplasia and migration of squamous epithelial cells were noted. The authors warn that heterotopia may easily be mistaken for metaplasia. Two cases of mammary tumors were found in those which received estrogen (no details; 27 mice were given M + estrogen, 11 received estrogen alone).

64-458 EXPERIMENTAL TUMORS OF THE PENIS. (Rus.) Shabad, A. L. (Clin. Urol., Centl. Inst. Postgrad. Med., Moscow). *Biull. eksp. Biol. Med.* 56(12):73-79, 1963.

After topical application of 9,10-dimethyl-1,2-benzanthracene (0.1-1.0% in benzene) to the glans penis and prepuce of rabbits, the agent was further confined by artificial phimosis in 1/12. After up to 110 applications every 2 days during up to 7 mo. there were macroscopically evident tumors in 7/8 survivors. Among 4 that died from a viral infection, besides epithelial hyperplasia of the glans and prepuce there was infiltrating papillomatous growth on the glans in 1 case. There was cancer of the prepuce and body of the penis in 5; papilloma of these regions in 7 and focal epithelial proliferations in 8. The first macroscopic evidence of tumors

was on the skin of the scrotum, 4 mo. after initiation of treatment.

64-459 PREVENTION OF CARCINOMA OF THE CERVIX. (E.) Stein-Werblowsky, R. (Roy. Veterin. Coll., London, N.W.1). *Lancet* 1:382-383, 1964.

When the vaginas of 106 rats were painted with 3,4-benzpyrene during the estrus or the diestrus, animals in diestrus developed cancer of the cervix (2), thymoma (1), leukemia (1), bile-duct carcinoma (1), and various benign lesions (14), whereas only 4/53 animals in estrus developed benign lesions. The author noted that cancer of the cervix was extremely rare in animals which mate only in estrus.

64-460 EXPERIMENTAL SQUAMOUS METAPLASIA AND SQUAMOUS EPITHELIOMA FORMATION IN THE PITUITARY OF THE RAT. (E.) Cheetham, H. D. (Dept. Bacteriol., U. Liverpool, England). *Brit. J. Cancer* 17(4):657-662, 1963.

When pellets of 9,10-dimethyl-1,2-benzanthracene (DMBA; 5% in cholesterol; 1-5 mg for 1 wk.-5 mo.) were inserted into the pituitary of 40 male and female 3-5-month-old Wistar rats, all the animals showed inflammatory changes in the tissues in and around the pellet and the pituitary of 8 animals also showed stratified squamous epithelium in various degrees of development according to the length of implantation. Of these animals, 2 showed typical squamous carcinomas extending into the hypothalamus, but no metastases were seen. One female rat also developed a s.c. adenocarcinoma. Pellets of cholesterol implanted into the pituitary of 6 rats produced very little inflammatory changes and were surrounded by a thin fibrous capsule usually lined with multinucleated giant cells, but no squamous change was produced. Linen thread implants provoked mild granulomatous reaction; extra-meningeal implants caused marked inflammatory reactions. The squamous epithelium appears to develop by metaplasia of pituitary cells and probably originates from the lining of the cleft between the anterior and intermediate lobes.

64-461 EXPERIMENTAL STUDIES ON THE GENESIS OF CARCINOMA OF THE LUNG. (Ger., Abstract) Dontenwill. *Med. Welt* 64(1):65, 1964.

Spraying tobacco smoke condensate as an aerosol into the tracheal tree of golden hamsters for long periods of time (up to >1 yr.) caused metaplastic changes in the epithelium of bronchi and trachea as well as papillary, noninfiltrative tumors of the air passageways. No carcinomas were found, but spontaneous adenomatosis of the lungs increased. Exposure to the smoke of 16 cigarettes/day caused slight metaplasia and papillary epithelial proliferation. The action of nitrosamine inj. was potentiated by smoke and smoke condensate; thus, since the spontaneous tumor rate was increased, smoke had a cocarcinogenic action.

- 64-462 METABOLIC PRODUCTS OF AROMATIC AMINES AS CANCER PRODUCING FACTORS. (Ger., Abstract) Uehleke. *Med. Welt* 64(1):65, 1964.

The metabolic products of drugs and impurities may be more active biologically than the original substances, e.g., after feeding acetylated amines, N-hydroxy compounds (which are stronger carcinogens than the amine itself) can be demonstrated in the urine. Enzymatic N-hydroxylation of various amines was carried out *in vitro* with isolated liver microsomes; the arylhydroxylamines produced could react just like alkylating agents with protein and (probably) also with the bases of nucleic acids. This supports the view that the carcinogenicity of aromatic amines depends on their N-hydroxylation during metabolism.

- 64-463 POSSIBLE CHONDROGENIC TRANSFORMATION OF BENZOPYRENE-INDUCED SARCOMA. (It.) Pentimalli, G. (Dept. Orth., U. Rome). *Ortop. Traumat. (Rome)* 31(4):379-389, 1963.

In albino Wistar rats the s.c. or i.p. inoc. of a mixture consisting of homogenates of 3,4-benzopyrene-induced sarcoma and rat embryos (with removal of all ectodermic and splanchnic portions) resulted in tumors which significantly differed from the original benzopyrene sarcoma. The new tumors were myxosarcomas, with a definite predominance of mature and immature fibroblastic cells and with a high degree of cellular atypia, monstrosities and mitotic figures. In some zones, the tumoral stroma showed vascular alterations similar to those of angiosarcomas. Characteristic of the tumor was the presence of islets and nodules of embryonal cartilaginous tissue. The latter was ascribed to the survival of young cartilaginous nodules existing already at the time of transplantation rather than to a chondroblastic transformation within the transplanted tumor.

- 64-464 EVALUATION OF THE CARCINOGENICITY OF AMINOFLUORENOLS BY IMPLANTATION INTO THE BLADDER OF THE MOUSE. (E.) Irving, C. C. (VA Admin. Hosp., Minneapolis, Minn.), H. R. Gutmann and D. M. Larson. *Cancer Res.* 23(11):1782-1791, 1963.

A more complete presentation of the paper previously abstracted as CRA 1(5):#827, 1963.

- 64-465 MACROCYCLIC DITERPENE HYDROXY ETHERS FROM TOBACCO AND CIGARETTE SMOKE. (E.) Rowland, R. L. (Dept. Res., R. J. Reynolds Tobacco Co., Winston-Salem, N. C.), A. Rodgman, J. N. Schumacher, D. L. Roberts, L. C. Cook and W. E. Walker, Jr. *J. Organ. Chem.* 29(1):16-21, 1964.

A description of three diterpenes isolated from

tobacco and cigarette smoke is presented. They have been characterized as 12-isopropyl-1,5,9-trimethyl-5,8-oxido-3,9,13-cyclotetradecatrien-1-ol and the α - and β -diastereoisomers of 12-isopropyl-1,5-dimethyl-9-methylen-5,8-oxido-3,13-cyclotetradecadien-1-ol by correlation with the previously described α -4,8,13-duvatriene-1,3-diol.

- 64-466 ANALYSIS AND DETERMINATIONS OF THE POLYCYCLIC HYDROCARBONS IN THE ATMOSPHERIC PARTICULATES OF THE CITY OF ROME. I. DETERMINATION OF 3,4-BENZOPYRENE. (It.) Valori, P. ("G. Sanarelli" Inst. Hyg., U. Rome), C. Melchiorri and N. Vescia. *Nuovi Ann. Ig. Microbiol.* 14(6):434-459, 1963.

The concentration of 3,4-benzopyrene in the atmospheric particulates of the city of Rome during the yr. 1962-1963 for the mo. of December, January, February and March was (in $\mu\text{g}/100 \text{ m}^3$ of air): 13.17, 14.54, 11.5 and 5.34, resp. Comparable figures for 1,12-benzoperylene were: 11.78, 16.6, 9.5 and 5.27. These values are similar to those observed in other cities in Italy or in other countries that have a higher level of industrialization. House heating systems are considered to be one of the main sources of the above air contaminants.

- 64-467 FURTHER STUDIES ON THE INFLUENCE OF ARENE-TYPE HYDROCARBON AIR POLLUTANTS ON *BACILLUS MEGATERIUM*. (E., Abstract) Won, W. D. (Sanit. Eng. Res. Lab., U. California, Berkeley) and J. F. Thomas. *Bact. Proc.* 1964:35.

Examination of cultures of *B. megaterium* grown under anaerobic conditions and maintained in defined media supplemented with a carcinogenic arene (3,4-benzopyrene, 20-methylcholanthrene, or 9,10-dimethyl-1,2-benzanthrene) showed considerable proportions of atypical morphological forms and the acceleration of oxidase activities, particularly that of reduced diphosphopyridine nucleotide oxidase. While abnormal forms were not apparent in cultures exposed to a noncarcinogen (phenanthrene, chrysene and anthracene), the enzyme-enhancing effect was exhibited to a lesser degree in cultures supplemented with phenanthrene and anthracene.

- 64-468 THE EFFECT OF EPSILON-AMINOCAPROIC ACID ON THE INDUCTION AND GROWTH OF SARCOMA INDUCED BY BENZ(a)PYRENE. (It.) Diomede-Fresa, V. (Inst. Gen. Path., U. Bari, Italy) and D. Fumarola. *Tumori* 50(1):25-30, 1964.

The admin. to Wistar albino rats of both sexes (3-month-old) of 3,4-benzopyrene (BP; 0.5% in almond oil s.c., 1 ml every 20 days x 3) alone (15 rats) or in conjunction with epsilon-aminocaproic acid (500 mg/dose x 3 s.c.) (15 rats) resulted in the development of s.c. sarcomas in all rats. In animals treated with both compounds, tumors

appeared earlier (av. 83.2 days) than in those receiving BP alone (av. 104.1 days), the survival time after the tumor appearance was shortened (av. 37.9 days vs. 42.3 days) and tumors were larger (av. 64.1 g vs. 40.6 g).

4-469 THE IDENTIFICATION OF NITRO-OLEFINS IN THE COMBUSTION PRODUCTS OF HYDROCARBONS. (E.) Lampe, K. F. (Dept. Pharm., U. Miami Sch. Med., Coral Gables, Fla.) and W. B. Deichmann. *Industr. Med. Surg.* 33(5):281-283, 1964.

Both a conjugated and nonconjugated nitro-olefin were formed when isobutylene (a pure hydrocarbon with both unsaturation and side-chain alkylation) was burned in an internal combustion engine. The products identified by gas chromatography were nitro-2-methyl-1-propene and its tautomer.

4-470 ROLE OF THYMUS AND THYMUS FACTORS IN THE INDUCTION OF 20-METHYLCHOLANTHRENE: IN CANCER IN MICE. (E.) Maisin, J. H. F. (Dept. Carcinogenesis, U. Louvain, Belgium). *Nature (London)* 202:202, 1964.

White mice (L Strain), 50% male and 50% female, were painted 3x/wk. for 7 wk. with a 0.25% soln. of 20-methylcholanthrene (MC) in ether and divided into 3 groups of 80 mice each. Group 1 mice were kept as controls; Group 2 mice were given thymal thymus grafts 3 times at 2 wk. intervals before MC painting; afterwards during the paintings and for the whole period of observation (10 days) similar grafts were given every 14 days. Group 3 mice were inj. with thymus homogenate. The number of mice with skin cancer after 60, 90, 120, 160, 180 and 210 days were, resp., 2, 9, 22, 35, 46 and 53 for Group 1; 0, 1, 26, 24 and 34 for Group 2; 0, 0, 8, 16, 24 and 32 for Group 3. The restoration of immune response by the thymus is considered as a possible mechanism of thymus-inhibiting action on MC-induced skin cancer in mice. (See also CRA 1(9-10): 13, 1964.)

4-471 IMMUNOPROPHYLAXIS OF INDUCED EXPERIMENTAL HEPATOMA. (E.) Maisin, J. H. F. (Dept. Carcinogenesis, U. Louvain, Belgium). *Nature (London)* 202:202-203, 1964.

Two groups of 50 rats (4 mo. old, wt. 140-170 g., 25 male and 25 female) were fed regular diets supplemented with 0.25% dimethylaminoazobenzene (DAB). Group 1 rats received no previous treatment and were kept as controls; Group 2 rats had previous inj. of lysosome fraction of DAB hepatoma; Group 3 rats had 5 previous inj. of microsome fraction of DAB hepatoma; Group 4 rats had previous inj. of supernatant of DAB hepatoma; Group 5 rats had inj. of microsome fraction of normal liver. Only the rats of Group 3 showed significant state of immunity (number of tumors after 16, 20, 25, 30, 35, 40 and 45 wk. was 0, 0,

0, 1, 3, 7, and 9, resp.); after 50 wk. there were 29 survivors. For comparison, among 17 50+ wk. survivors of Group 2 results were 1, 1, 1, 5, 10, 12 and 15; among 19 50+ wk. survivors of Group 5 results were 0, 0, 0, 1, 7, 11 and 15; among 16 50+ wk. survivors of Group 1 results were -, -, 1, 4, 9, 14 and 19. (For related study, see CRA 1(6):#1065, 1963.)

64-472 IMMUNOPROPHYLAXIS OF EXPERIMENTAL CANCER. (Fr.) Maisin, J. *Bruxelles Med.* 44(12):323-335, 1964.

The author reviews the results of several studies which were previously reported in CRA 1(6):#1065, 1963; *ibid.*, 2(3):#470, and *ibid.*, #471, 1964.

64-473 THE ROLE OF THE THYMUS AND SPECIFIC ANTIGENS IN 20-METHYLCHOLANTHRENE-INDUCED CANCERS. (Fr.) Maisin, J. H. F. (Cancer Inst., Cath. U., Louvain, Belgium). *C. R. Soc. Biol. (Paris)* 157(7):1519-1522, 1963.

See CRA 1(6):#1065, 1963; *ibid.*, 2(3):#470 and *ibid.*, #472, 1964.

64-474 ETHANOL AND THE CARCINOGENICITY OF N-HYDROXY-N-2-FLUORENYLACETAMIDE IN MALE AND FEMALE RATS. (E., Abstract) Weisburger, J. H. (NCI, Bethesda, Md.), R. S. Yamamoto and S. R. Pai. *Toxic. Appl. Pharmacol.* 6(3):363, 1964.

Group 1 of weanling male and female NIH Black rats were fed a semisynthetic 18% casein diet and water; Group 2, the diet + 10% ethanol (EtOH); Group 3, the diet + 0.008% N-hydroxy-N-2-fluorenylacetylamide (N-OH-FAA) and water; Group 4, the diet + N-OH-FAA and 10% EtOH. After 10 mo. the animals were grossly normal. After 14 mo. Groups 3 and 4 had enlarged livers, spleen and adrenals and lower hematocrit values; Groups 2 and 4 had heavier testes; the livers of all rats in Groups 3 and 4 had cysts. Hepatomas with no cholangioma were found in 8/15 and 9/13 males in Groups 3 and 4. Hepatomas were found in 8/17 and 10/17 in females of Groups 3 and 4; cholangiomas were seen in 8/17 and 11/17, resp. Few rats had both lesions. Treatment with EtOH appeared to have a slight moderating effect on the carcinogenicity of the low level of N-OH-FAA used, as demonstrated by the smaller size of tumors.

64-475 CONTRIBUTION TO CARCINOGENESIS. (E.) Košir, A. (Dept. Histol. Embryol., Fac. Med., U. Ljubljana, Yugoslavia). *Acta Med. Jugosl.* 16(2):43-49, 1964.

See CRA 1(5):#859, 1963.

64-476 TRACE ELEMENTS AND LEUKAEMIA. (E.) Questions and Answers. *Brit. Med. J.* 1:1237, 1964.

While no definite association has been proven between the absence or presence of trace elements in the etiology of leukemias, there is a large amount of evidence of the occurrence of various blood dyscrasias. The author had seen a leukemic picture after the taking of or exposure to lead and arsenic, and a case of agranulocytosis terminating as an acute leukemia after exposure to lead associated with sulfonamide therapy.

- 64-477 MITOTIC RATE OF METHYLCHOLANTHRENE INDUCED SUBCUTANEOUS FIBROSARCOMA. (E.) Bertalanffy, F. D. (Dept. Anat., U. Manitoba Sch. Med., Winnipeg, Canada). *Naturwissenschaften* 50(20):648-649, 1963.

Tumors were induced in Holtzman-Sprague-Dawley rats by inj. of 20-methylcholanthrene (0.1 ml, 1% soln. 2x/wk. s.c.) into the back. First tumors appeared at the site of inj. after 34 inj. and by 6 mo. nearly all rats developed fibrosarcomas. Mitosis was measured by the colchicine method (0.1 mg/100 g body wt.; animals were sacrificed 6 hr. later). The 24-hr. mitotic rate of the MC-induced fibrosarcoma was 9.41%. Once the tumor was initiated, the rate of growth was constant at 0.4% new cells/hr., day and night.

- 64-478 IN VITRO CELL TRANSFORMATION WITH CHEMICAL CARCINOGENS. (E.) Berwald, Y. (Weizmann Inst. Sci., Rehovoth, Israel) and L. Sachs. *Nature (London)* 200:1182-1184, 1963.

Golden hamster and C57BL/6 mouse embryo cells (1×10^4 or 5×10^4 cells/plate) were treated with 3,4-benzpyrene (BP) or 20-methylcholanthrene (MC; both in paraffin disks containing 5% of the carcinogen heated to 180°C) before, at the time of or after cloning, or with urethan (U; 10 mg/ml) which was added directly to the culture medium 3 days before cloning; mass cultures were also infected in some experiments with the polyoma virus (PV) mutant SP2 (virus:cell ratio of 10 PFU/cell and 2 hr. of adsorption) before the cells were plated for cloning. Mass embryo cell cultures treated with BP for 9 days before cloning showed 17.8% transformed clones (random growth pattern and fusiform cell shape), while no transformed cells were seen in cultures pretreated for the same period with disks containing only paraffin. A reduction in the period of treatment to 2 days before cloning gave 5.2% BP transformed clones, and 8.3% with additional BP at time of cloning, compared with 1.3% PV transformed clones. The percentage of BP transformed clones with the various times of treatment ranged from 5.2-26.3% and for PV transformed clones, 0.2-1.3%. The results indicate that cell transformation was induced as a direct action of the carcinogen. Similar results were obtained after MC treatment of hamster embryo cells and after BP and MC treatment of mouse embryo cells. No transformed clones were seen in a total of about

2400 hamster embryo clones and 960 mouse embryo clones examined after treatment with U. The results seem to indicate the feasibility of studying cell transformation by chemical carcinogens in vitro.

- 64-479 A METHOD FOR STUDYING EMBRYONAL TOXIC AND TERATOGENIC EFFECTS IN RATS. (Ger.) Lorke, D. (Inst. Toxicol., Farbenfabriken Bayer A. G., Wuppertal-Elberfeld, Germany). *Naunyan-Schmiedeberg. Arch. Exp. Path.* 246(2):147-151, 1963.

As a method of determining toxic and teratogenic drug effects on rat embryos, the author recommends dating the time of conception by means of the presence of sperm in daily vaginal smears, anesthetizing the female 20.3 days later and removing the embryos alive. A method for making the embryonal skeleton clearly visible (after Dawson) is also detailed. Mean tabulations of wt. gain during pregnancy, number of ova fertilized, number of fetuses per litter, number of fetal resorptions per litter, and fetal wt. are given for untreated rats of the Elberfelder strain (random-bred Strain FB 30).

- 64-480 PHYSIOLOGICAL GENETICS OF MELANOTIC TUMORS IN DROSOPHILA MELANOGASTER. II. THE GENETIC BASIS OF RESPONSE TO TUMORIGENIC TREATMENTS IN THE tu^k AND tu^{bw}; st su-tu STRAINS. (E.) Burnet, B. (Agric. Res. Coun., Poultry Res. Ctr., Edinburgh, Scotland) and J. H. Sang. *Genetics* 49(2):223-235, 1964.

In inbred tu^k and tu^{bw}; st su-tu strains of Drosophila melanogaster, which have a low incidence of melanotic tumors (in the larvae) when cultured on a chemically defined medium under germfree conditions, omission of RNA from the medium caused a significant increase in tumor penetrance in the tu^k strain (81.4% of the individuals showing tumors compared to 1.3% of the controls) but not in the tu^{bw} strain (12.6%, controls 12.2%) or in the F₁ of the reciprocal crosses between the two strains (1.79%, controls 0%). Low cholesterol in the medium (0.00156%) caused a sharp increase in tumor penetrance in both strains (77.4% in tu^k and 84.5% in tu^{bw}) but not in the F₁ (2.96%). Addition of tryptophan (0.9%) to the medium resulted in the appearance of melanotic tumors in the majority of treated larvae (83.0% in tu^k, 94.5% in tu^{bw}, 94% in the F₁). X-ray treatment (1000 r) of 22-hour embryos caused increased tumor penetrance only in tu^{bw}; st su-tu (87.4%) along with appearance of the erupt phenotype. All treated groups had a low frequency of morphological variants of the head, thorax and legs. In backcrosses of the tumor strains with nontumor strains carrying dominant markers, flies carrying substituted chromosomes but still carrying chromosome #2 (with either the tu^k or tu^{bw} genes) had reduced penetrance. Only in the case of cholesterol deficiency does the third chromosome substitution significantly

duce tumor penetrance, disclosing the presence of a modifier specific to this treatment. Further analysis indicated that dietary-environmental treatments which increase tumor penetrance influence the reaction controlled by the tumor gene rather than cause interference with the action of a specific tumor suppressor. (See also CRA 1(11):#115, 1964.)

481 RECENT EXPERIMENTAL DATA ON THE CARCINOGENIC ACTIVITY OF ISONICOTINIC ACID RAZID (INH). (Hun.) Juhász, J. (Inst. Path. Exptl. Cancer Res., Med. U. Budapest), Baló and B. Szende. *Magy. Onkol.* 7(4):193-199, 1963.

CRA 1(8):#1489, 1963.

482 EXPERIMENTAL STUDY OF BRAIN TUMORS. (Jap.) Kawai, S. (Dept. Path., Gumma U. Med., Japan). *Nippon Byorigaku-kai Kaishi Jans. Soc. Path. Jap.* 52:59-82, 1963.

Methylcholanthrene pellets (described as 2 g wt. and 2 mm in length) were inserted in the cortex of the cerebrum, the cerebellum and meninges of a total of 344 mice of various strains and 212 rats (54 Wistar, 158 Donryu). Tumors were found in 112/242 mice which survived and 94 days after insertion: 39 glioma, 63 mesenchymal, 8 mixed glio-mesenchymal, 2 unknown. Tumors were found in 21/121 Donryu rats which survived over 90 days: 13 glioma, 1 gliosarcoma, 1 mesenchymal and 1 epidermoid; none occurred in control rats. In mice, total tumor incidence according to strain was: C3H (after 94 days) 57/118 (48.3%); C57B (135 days) 25/56 (44.6%); ddN (116 days) 20/33 (60.6%); CF (238 days) 3/12 (25%); B6 (96 days) 7/15 (46.7%). After s.c. and/or intracerebral isologous transplantation of the excised tumors in the mouse, incidence of successful takes was: 19/26 glioma, 4/4 gliosarcoma, 7 sarcoma and 1/1 meningioma. In the rat 5/10 glioma and 1/2 meningioma were successfully transplanted. Heterologous transplants (intracerebral or aqueous humor) were successful in 2/9 mice and 2/4 rats. This study revealed a high incidence of mesenchymal tumors. (See also CRA 1(11):#17, 1964.)

483 CARCINOGENIC SUBSTANCES IN WATER AND SOIL. AN INTERIM REPORT. (Ger.) Hoff, J. (Inst. Hygiene, U. Mainz, Germany). *Hyg. Bakt.* 148(1):1-11, 1964.

of a report on various levels of carcinogenic substances (polycyclic aromatic hydrocarbons of benzopyrene, benzfluoranthene, benzanthracene, indeno-pyrene types) found in wells, rivers, lakes, plankton, dust and soil samples in Germany. Based on animal experiments, it is believed that the cumulative effect of at least 30 g suggested carcinogens would be required to have

an effect on humans, but that intake of such a quantity is highly unlikely, even in a period of many years. River waters were found to be most contaminated. (The Rhine at one site yielded 60 g solids/2.6 cubic meters of water, with an active carcinogen content of 3.0 mg/kg; while samples from other rivers showed active carcinogen contents of 4.0-20.0 mg/kg of retrievable solids.) Filtration through activated charcoal has proved effective in purifying the water; chlorination has not. Some comments on the possible decomposition of these carcinogens (e.g., by ozonization) or their biosynthesis (through plankton) are also included. (For other parts of this report, see CRA 1(3):#412, *ibid.*, 1(6):#1066, *ibid.*, 1(7):#1235, 1963 and *ibid.*, 1(9-10):#1696, 1964.)

64-484 THE CARCINOGENIC ACTION OF AFLATOXIN AFTER ITS SUBCUTANEOUS INJECTION IN THE RAT. (E.) Dickens, F. (Middlesex Hosp. Sch. Med., London, W.1) and H. E. H. Jones. *Brit. J. Cancer* 17(4):691-698, 1963.

In male rats (wt. 100 g) inj. s.c. into the right flank with a crystalline preparation of aflatoxin (50 µg/0.5 ml arachis oil 2x/wk. x at least 50 wk. or 500 µg 2x/wk. x 8 wk.) containing 37.7% aflatoxin B₁ and 56.4% aflatoxin G₁ (obtained from cultures of *Aspergillus flavus*), there was little difference between the tumor incidence (6/6 and 5/5, resp., developed tumors at inj. site) or the earliest tumor appearance (20 and 21 wk.) in rats treated with 50 or 500 µg. No tumors occurred in control rats given only arachis oil (0.5 ml s.c.). All the tumors were typically sarcomas or fibrosarcomas and varied greatly in their proliferative activity and their ability to grow on transplantation. No malignant changes were seen in the liver and lymph nodes, although 1 animal treated with 16 inj. of 500 µg showed necrosis of the liver parenchyma. At the time of report, a group of 20 mice and 20 oil-treated controls were receiving aflatoxin (10 µg in 0.1 ml arachis oil 2x/wk. x 12) but showed no tumors. (See also CRA 1(5):#872, 1963.)

64-485 SIALIC ACID CONTENT OF NORMAL RAT LIVER AND OF DAB-INDUCED HEPATOMATA. (E.) Kalant, H. (Dept. Pharm., U. Toronto, Ontario, Canada), W. Mons and M. Guttman. *Canad. J. Physiol. Pharmacol.* 42(1):25-31, 1964.

In male and female Wistar rats bearing hepatomas (mostly adenocarcinomas) induced by the feeding of dimethylaminoazobenzene (DAB; 0.06% in a low protein diet for 4 mo.), the total sialic acid content (determined by acid hydrolysis isolation on Dowex-2 columns and reaction with thiobarbituric acid) of the tumor was an av. of 1162 µg of neuraminic acid/g of tissue while the surrounding liver and the necrotic tumor contained 587 µg/g and 922 µg/g, resp.; normal rat liver contained 465 µg/g. Treatment of tissue sections with purified neuraminidase liberated only 27-28% of the sialic acid

from liver tissue but 49% of that in the hepatoma. Paper chromatography revealed that the sialic acids from normal liver contained mainly N-acetylneuraminic acid as well as an unidentified fast moving component with little or no N-glycolylneuraminic acid, while tumor sialic acids were composed entirely of N-acetyl and N-glycol derivatives and no fast moving component was detected. Possible explanations for the elevated sialic content of the hepatomas were discussed.

- 64-486 THE HISTOGENESIS OF EXPERIMENTALLY PRODUCED MELANOTIC TUMOURS IN THE CHINESE HAMSTER (*CRICETULUS CRISEUS*). (E.) Ghadially, F. N. (Dept. Path., U. Sheffield, England) and O. Illman. *Brit. J. Cancer* 17(4):727-730, 1963.

When the shaved skin in the area of the left flank around the costo-vertebral (C.V.) spot of Chinese hamsters (2 male, 6 female, wt. = approx. 40 g) was painted with 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.2% in acetone, 1x/wk. x 37), a few keratoacanthomas were seen and 6/8 animals developed multiple melanotic tumors beginning at wk. 11 which were oval, elongated, or band shaped (only a few were spherical) and were distributed around the C.V. spot. These tumors arose from a diffuse dermal network of melanocytes surrounding many pilosebaceous follicles or from small perifollicular networks similar to those of the Syrian hamster. Therefore, the C.V. spot was resistant to carcinogenesis.

- 64-487 PHOTOCHEMICAL ADDITION OF BENZO(a)PYRENE TO PYRIMIDINE DERIVATIVES. (E.) Rice, J. M. (Dept. Chem., Harvard U., Cambridge, Mass.). *J. Am. Chem. Soc.* 86(7):1444-1446, 1964.

3,4-Benzpyrene (BP) formed stable addition products with uracil, thymine, cytosine, 5-methylcytosine, guanine and 6-azathymine when irradiated with UV light. A conjugated carbonyl group within the pyrimidine ring is essential for the reaction which occurs in 4% aqueous sodium dodecyl sulfate (SDS) with 0.0001 M hydrocarbon and 0.032 M pyrimidine in quartz cuvettes at pH 6-7. This photo-addition of BP to ribo- and deoxyribonucleosides and denatured salmon sperm DNA was seen directly by the UV absorption of the pyrimidine photo products in SDS soln. containing 0.2 M NaOH.

- 64-488 THE RESPONSE OF EXPERIMENTALLY INDUCED MAMMARY TUMOURS IN RATS TO OVARIECTOMY. (E.) Daniel, P. M. (Dept. Neuropath., Maudsley Hosp., London, S.E.5) and M. M. L. Prichard. *Brit. J. Cancer* 17(4):687-690, 1963.

When female 42-79-day-old Sprague-Dawley rats were admin. 20-methylcholanthrene (MC; 10 mg in olive or sesame oil 3x/wk. x 7 wk. via stomach tube), adenomatous mammary tumors developed at various times from wk. 4 on. When the tumors reached 1-3 cm in diameter, ovariectomy was

performed and the number of animals showing complete regression, some regression and no regression after 16 days-25 wk. was 6/13, 4/13 and 3/13, resp. These results indicate that ovariectomy was somewhat less effective than previously published results on regression of MC-induced tumors by hypophysectomy, but ovariectomy was more effective than pituitary stalk section.

- 64-489 HOMOLOGOUS TUMOUR GROWTH IN METHYLCHOLANTHRENE-INDUCED SARCOMA-BEARING MICE. (E.) Matsuyama, M. (Dept. Path., Nagoya City U. Sch. Med., Japan) and T. Nakamura. *Nature (London)* 202:200, 1964.

Host resistance against tumor transplants was diminished in mice bearing methylcholanthrene-induced fibrosarcomas. Female SM strain mice inj. s.c. with 0.1 mg 20-methylcholanthrene in olive oil developed fibrosarcomas 12-15 mm in diameter within 11-18 wk. Cells of MSN fibrosarcoma (initially induced by urethan in Tween 80 in dd/N mice) were then inj. s.c. Group A (17 mice) received 10^4 cells of the 7th transfer generation, Group B (18 mice) received 9×10^5 cells of the 8th transfer generation. In 10/17 of Group A in which progressive tumors developed, the rate of tumor growth was 59% of that in the donor animals (vs. 0% in similarly challenged, normal controls) and the mice showed a lesser degree of splenomegaly than those in whom progressive tumors failed to develop. In 18/18 of Group B, the rate of tumor growth was approx. 100% of that in donor animals, vs. 0% in similarly challenged, normal controls. In both groups controls developed barely palpable MSN tumors immediately after challenge, which disappeared spontaneously within 3 wk. (See also CRA 1(3):#397, 1963.)

- 64-490 BRAIN CONTENT OF AMMONIA, GLUTAMINE AND GLUTAMIC ACID IN RATS BEARING EXTRA-CEREBRAL SARCOMA. (Rus.) Rogoznaia, A. V. (Res. Inst. Radiol. Oncol., Rostov-on-Don, USSR). *Vop. Med. Khim.* 10(1):44-47, 1964.

The amount of ammonia in the brain of rats with procaine-synestrol-induced sarcoma increased with the development of the tumor, and decreased toward the end of growth, approaching normal values. Glutamine first increased markedly, decreased at the peak of tumor growth and increased again toward the end of the period of growth. Glutamic acid content was the same as in controls at first, then decreased with tumor growth, and became normal toward wk. 3-4. The accumulation of ammonia, according to the author, is indicative of disturbed metabolism in the process of growth of procaine-synestrol-induced sarcoma.

- 64-491 A STUDY OF THE CARCINOGENIC ACTIVITY OF A SINGLE INJECTION OF 7,12-DIMETHYLBENZ[a]ANTHRACENE INTO NEWBORN C57BL MICE. (E.) Baroni, C. (Inst. Anat. Path. Histol., U. Pavia,

aly) and F. Cefis. *Tumori* 49(6):373-378, 1963.

ter inj. within 16 hr. of birth of C57BL mice with 9,10-dimethyl-1,2-benzanthracene (100 µg, c.) only 38/165 (23%) survived weaning (6 wk.) contrast to 76% in untreated controls. Of these survivors, 60.5% (16 males, 7 females) developed the following tumors: 4 malignant thymic lymphomas (4 males; av. latent period (LP) approx. 5 wk.); 6 s.c. tumors at the site of inj. (3 male, 3 female; av. LP 26 wk.); 5 skin tumors (1 male, 2 female; av. LP 50 wk.); 7 liver hemangiomas (5 male, 2 female; av. LP 54 wk.); 2 cardiac hemangiomas (2 male; LP 55 wk.); 1 liver hemangiosarcoma (1 female; LP 55 wk.); 3 lung adenomas (1 male, 2 female; av. LP 55 wk.); 1 cholangioma (1 male; LP 55 wk.); 1 hepatoma (1 male; LP 95 wk.). Of 102 controls (76%) still alive at 6 wk. of age, 5.9% (3 male, 3 female) developed the following tumors: 4 generalized malignant lymphomas (1 male, 3 female; av. LP 55 wk.), 1 lung adenoma (1 male; LP 66 wk.), and 1 hepatoma (1 male; LP 95 wk.). These results indicate that DMBA, given s.c. at birth, has a lower carcinogenic activity in C57BL mice than other strains.

492 EFFECT OF DURATION OF EXPOSURE ON NICKEL SULPHIDE TUMORIGENESIS. (E.) Chen, H. (Ontario Vet. Coll., Guelph, Canada) and J. P. W. Gilman. *Nature (London)* 202: 1307, 1964.

id disks of pressed nickel sulfide (8 mm x 1 mm, wt. 250 mg) were implanted into the right scapular region of inbred Fischer rats and removed at 2, 4, 8, 16, 32, 64, 128 and 256 days afterwards. With disk exposure times of 2-32 days no tumors resulted, while with disk exposure times of 64, 128 and 256 days tumors developed in 4/10, 0, and 10/10, resp., effective animals (animals surviving longer than the shortest latency period encountered); av. latency periods were, 191, 205, and 230 days. Besides palpable tumors, histological changes of an early carcinomatous nature and suggesting early rhabdomyosarcoma were observed in 4/5, 1/5 and 0/5 animals killed at 128, 256, and 64 days, resp. No cancers developed in response to equal-sized disks of ferric oxide implanted into the opposite hip of each animal and removed at the same times as the nickel sulfide disks.

493 PRELIMINARY OBSERVATIONS ON THE CARCINOGENIC ACTIVITY OF 4,4'-DINITROBIPHENYL. (E., Abstract) Laham, S. (Food Drug Inspectorate, Dept. Natl. Health Welfare, Ottawa, Canada), H. C. Grice, and J. W. Sinclair. *Toxicol. Pharmacol.* 6(3):352, 1964.

ed feeding of 5 mg of 4,4'-dinitrobiphenyl (4,4'-DNB; 5 mg in oil/wk. x 8) to 16 female and 16 male Sprague-Dawley rats (starting at age 5 weeks), with doses subsequently increased to 10 mg

for several wk. (discontinued in females because of its toxic effects) produced during 42 wk. of observation tumors only in 12 females: squamous cell carcinoma of the ear duct in 5, mammary adenocarcinoma in 5, salivary gland carcinoma in 1 and undifferentiated carcinoma of the abdomen in 1. Pulmonary adenoma was seen in a rat already presenting a mammary adenocarcinoma and skin hamartoma. The av. cumulative intake of 190 mg/rat of 4,4'-DNB necessary to induce a significant percentage of malignant tumors was far below the amount necessary with other nitro derivatives of biphenyl. Present studies indicate 4,4'-DNB is a more active carcinogen than 4-nitrobiphenyl and 2,2'-dinitrobiphenyl.

64-494 ASPECTS OF THE ELECTRONIC STRUCTURE OF NEW TYPES OF AROMATIC CARCINOGENIC COMPOUNDS. (Fr.) Pullman, A. (Biol. Phys. Chem. Inst., U. Paris). *C. R. Acad. Sci. (Paris)* 257(1):288-290, 1963.

The energetics and electronic structures of benzo(j)fluoranthene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(m,n,o)fluoranthene, benzdehydro-15,16-cholanthrene and tricycloquinazoline are presented. Particular note is made of the fact that planar benzo(m,n,o)fluoranthene lacks carcinogenic activity, whereas non-planar 3,4-benzophenanthrene has carcinogenic properties. (See CRA 2(3):#495 and *ibid.*, #496, 1964.)

64-495 ASPECTS OF THE ELECTRONIC STRUCTURE OF THE NUCLEIC ACIDS IN RELATION TO THE THEORIES OF MUTAGENESIS AND CARCINOGENESIS. (E.) Pullman, B. (Biol. Phys. Chem. Inst., U. Paris). Pp. 141-159 in *Biopolymers. Quantum Aspects of Polypeptides and Polynucleotides*. Sym. 1. Stanford U., Cal. March 25-29, 1963. Weissbluth, M. (Ed.). Interscience Publ., Easton, Pa., 565 pp., 1964.

With the application of the molecular orbital method of quantum chemistry the author develops further evidence that mutagenesis and carcinogenesis arise from similar molecular activity (see CRA 1(9-10):#1708, 1964). Firstly, such molecules as alkylating agents and planar aromatic chemicals can give rise to both. Secondly, the mutagenic mechanism of aminoacridine's interaction with nucleic acids producing intercalation between 2 successive complementary pairs of the purine-pyrimidine bases and untwisting the phosphate-deoxyribose backbone, provides a model for this theory. It is suggested that aromatic hydrocarbons react similarly (probably at the K-L region) producing tautomeric shifts and disorganizing DNA bases, thus giving rise to genetic alterations which induce carcinogenesis. Charge-transfer formation may be the force in this interaction since the solvent power of a series of purines to a given hydrocarbon is paralleled by its electron donor property. In an addendum there is further discussion of the theory of Allison and Nash (see

CRA 1(9-10):#1708, 1964). (See also CRA 2(3):#496, 1964.)

64-496 THE THEORY OF CHEMICAL CARCINOGENESIS AND THE PROBLEMS OF HYDROCARBON-PROTEIN INTERACTIONS. (E.) Pullman, A. (Biol. Phys. Chem. Inst., U. Paris). Pp. 47-65 in Biopolymers. Quantum Aspects of Polypeptides and Polynucleotides. Sym. I. Stanford U., Cal. March 25-29, 1963. Weissbluth, M. (Ed.). Interscience Publ. Easton, Pa., 565 pp., 1964.

According to the author, carcinogenic aromatic hydrocarbons must possess a reactive K region in order to allow an electrophilic bond addition reaction and, if an L region exists, it could be appropriately indexed with activity. These conditions facilitate a hydrocarbon-protein interaction that might define chemical carcinogenesis. The following *in vivo* biochemical evidence found after skin application of such hydrocarbons clearly substantiates this theory: the formation of hydrocarbon-protein complex involving strong binding closely related to the induction of tumors, chemical inhibitors of carcinogenesis decrease the amount of complex formed, and the complex is only formed in tissues (e.g., epidermis) that develop tumors. Electrophoretic studies showed that all carcinogens are bound to a particular fraction of the protein (fraction I) and this binding involves the K region of the hydrocarbons. Preferring this evidence the author reviews and refutes theories based on physical properties (electron or excitation transfer). (See CRA 2(3):#495, 1964.)

64-497 GROWTH OF RAT LEUKEMIA BY ORAL FEEDING OF MALIGNANT TUMOR HOMOGENATE. (Jap., Abstract) Hamazaki, Y. (Natl. Okayama Hosp., Japan). Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.) 52:227-228, 1963.

Many fasted rats (50-70 g) fed orally 3-4 g fresh homogenate of NY reticulum cell sarcoma at 3-4-day intervals for more than 5 times developed signs of hypersensitivity, agitation and died of anemia. Homogenates of the spleen, lung and liver of these rats inj. i.p. into adult hybrid albino rats resulted in splenomegaly, adenopathy and in the appearance of lymphoblasts in the blood after 5-6 days. These rats died due to cachexia and anemia 2-4 wk. after inj. Rats which survived the oral feeding of tumor tissue showed tumors in the basilar meninges. When such a rat was sacrificed as soon as the tumor was apparent and the homogenate of its spleen was inj. i.p. into other rats, leukemia developed. However, if the tumor-bearing rat was sacrificed somewhat later, only the NY tumor was seen.

64-498 STUDIES ON EXPERIMENTAL BLADDER TUMOR: INFLUENCE ON THE MUCOUS MEMBRANE OF THE URINARY BLADDER OF THE CARCINOGENIC SUBSTANCE

9,10-DIMETHYL-1,2-BENZANTHRACENE. (Jap.) Kawai, T. (Dept. Urol., Yokohama U. Sch. Med., Japan). Hinyokika Kiyo (Acta Urol. Jap.) 9(11): 587-594, 1963.

The effect of 9,10-dimethyl-1,2-benzanthracene (DMBA) on the mucosa of the urinary bladder of rabbits was determined by surgically suturing on to it pieces of gauze on which was absorbed 30 mg of drug dissolved in 0.2 g of paraffin. In 7/10 16-month-old rabbits which could be followed after operation, foreign body calculi with salts of the carcinogen were found in 3 animals; in 4 the gauze was apparently resorbed. Among 8/10 survivors of 10-month-old rabbits, 3 showed papillary hyperplasia (without salt) of the mucosa 100 days after operation while 5 died within 2 mo. Intact rabbits showed no histological changes while operated rabbits with sutured gauze and paraffin without DMBA showed foreign body calculi in 2/3 and disappearance of gauze in 1/3 3 mo. after operation.

64-499 ANALYTIC IMMUNOELECTROPHORESIS IN THE STUDY OF SIMPLIFIED ANTIGENIC MOUSE LIVER STRUCTURE IN EARLY STAGES OF CARCINOGENESIS. (Rus.) Gel'shtein, V. I. (Inst. Clin. Exptl. Oncol., Acad. Med. Sci., Moscow) and T. A. Iagorskaia. Biull. Eksp. Biol. Med. 57(2): 90-93, 1964.

Analytical immunoelectrophoresis was employed to investigate the antigenic structure of the liver during early stages of carcinogenesis induced in C3HA mice of both sexes with o-aminoazotoluene (topically applied) and CCl₄ (s.c.). Serum from rabbits which were immunized with normal mouse liver and liver from mice at various stages of carcinogenesis showed the presence of 5 organ-specific antigens. However, the sera against precancerous liver showed antibodies against only 3 organ-specific antigens. To deplete the sera against precancerous liver lesser amounts of normal components were required than to deplete sera against normal liver. (See also CRA 1(12):#2078, 1964.)

64-500 STUDIES ON THE GENETIC MECHANISM IN CELL IMMUNITY. I. EXPERIMENTS ON THE TRANSFER OF DNA FROM A RESISTANT LEUKEMIA CELL LINE. (Rus.) Solov'ev, V. D. (Moscow Inst. Med. Min. Health RSFSR, Moscow), N. E. Gulevich, N. B. Varshaver, V. A. Otroshchenko and L. V. Volkova. Vop. Virus. 9(1):19-24, 1964.

DNA isolated from a leukemic cell line resistant to Coxsackie B3 virus and DNA from the original line highly susceptible to the virus both inhibited the cytotoxic effect of the virus when added to suspensions of cells of the original line. The DNA from the resistant line was the more effective of the two. When mixed directly with the virus, the two DNA preparations failed to neutralize it. Hence, it appears that the DNA acts in an indirect way, through cells. These

periments indicate that it may be possible to transfer from cell to cell cellular genetic material which is capable of influencing the susceptibility of the recipient cells.

-501 IMMUNOLOGIC BEHAVIOR OF THE LIVER IN THE COURSE OF EXPERIMENTAL CARCINOMATOSIS. (Fr.) Dufour, D. (Laval U., Quebec, Canada). Pp. 127-129 in Protides of the Biological Fluids. Proc. 11th Colloq. Bruges 1963. Peeters, H. (Ed.). Elsevier Publ. Co., Amsterdam, 526 pp., 1964.

vers of rats fed a diet with dimethylaminoazobenzene (DAB) or 2-acetylaminofluorene (AAF) for 9 mo., resp., showed the presence of a DAB- or a AAF-tumor-specific antigen. In a more advanced stage of carcinogenesis, a second antigenic factor was observed in the liver of both B- and AAF-fed rats which was identical with an antigenic factor previously found in the liver of a rat bearing Walker carcinoma. (For related studies see CRA 1(12):#2115, 1964.)

-502 SARCOMA PRODUCED BY SUBDERMAL ADMINISTRATION OF METAPHENYLENEDIAMINE AND o-PHENYLENEDIAMINE HYDROCHLORIDE. (E.) Kikuchi, N. (Dept. Hygienics, Kyushu U. Sch. Med., Fukuoka, Japan), S. Yamaguchi and T. Matsuoka. J. Med. Sci. 13(3):175-179, 1962.

Wistar-King rats were inj. s.c. every other day with 10% of the LD₅₀ of o-phenylenediamine (OPD; 45 mg/kg), m-phenylenediamine (MPD; 9 mg/kg) or m-phenylenediamine HCl (MPDH; 12 mg/kg), within 1 mo. a sarcoma developed in 1/5 of the animals treated with MPD, while no tumors occurred in the animals treated with OPD or MPDH and the controls. A sarcoma developed in 1/5 rats after 5 mo. of treatment with MPDH at 24 mg/kg s.c., but no tumors developed in animals treated with OPD (90 mg/kg) or MPD (18 mg/kg) and the controls. All tumors were located at the site of inj. and were composed of atypically proliferating fibroblasts and abnormally growing connective tissue which presented the picture of a fibrosarcoma. Other effects noticed were liver fat droplet infiltration and pigmentation in Kupffer's cells such as that seen in p-phenylenediamine poisoning, whereas in the kidneys, hyaline and other forms of regressive generation were seen; in the lungs pigmentation and pneumonic, emphysematous and atelectatic lesions occurred, while in the spleen deposition of hemosiderin and pigmentation were seen.

-503 ELECTRON MICROSCOPIC STUDY OF CHANGES IN HUMAN EPIDERMIS INDUCED BY TOPICAL APPLICATION OF 3,4-BENZOPYRENE. (It.) Meneghini, G. (Dept. Dermatol., U. Milan, Italy), G. Valentini and R. Caputo. Gior. Ital. Derm. 105(5):399-414, 1963.

Six pts. (age 48-65 yr.) with various skin conditions were treated with 3,4-benzopyrene (BP; 2% in benzene) topically on the arm (0.3 ml/painting) daily for up to 90 days. Macroscopically, hyperkeratosis and hyperpigmentation were observed only after 90 days of treatment with BP. Histological examination disclosed also changes in the deep layer of the epidermis, hyperpigmentation and dissociation of the cells of the basal layer and of the dermis, with dissociation of the collagen fibers. Electron microscopic studies showed a slight alteration of the basal membrane, lesions of the cytoplasmic membranes (especially in the basal and spinocellular layers which were followed by cellular dissociation and rupture and alterations of the desmosomes, prickly cell nuclei with segmented edges and peripheral thickening of chromatin especially in senile subjects), and swelling of mitochondria. Particularly interesting was the observation of the migration of dermal cells into the various layers of the epidermis. The earliest changes occurred in the spinocellular layer (after 10 days) and then in the basal membrane and basal and cornified layer (after 20 days). In 3 pts. treated with benzene alone, changes were qualitatively similar but quantitatively less than with BP; alteration of the prickly cell nuclei was not seen. Although BP was capable of inducing many changes of the fine structure epithelial cells, evidence of neoplastic transformation was lacking.

64-504 DRUG-INDUCED TUMORS OF THE THYROID IN GUINEA PIGS WITH EXPERIMENTAL THYROIDITIS. (E.) Hellwig, C. A. (Hertzler Clin. Res. Found., Halstead, Kan.) and J. W. Welch. Growth 27(4):305-315, 1963.

To demonstrate the influence of thyroiditis on the incidence of thyroid drug-induced tumors, 50 male guinea pigs were fed basic diets and treated as follows: Group 1, tap water + propylthiouracil (PT; 0.03% soln.) + thyroid-lipid extract (E; 1 ml/inj. x 7 s.c.); Group 2, PT alone; Group 3, E alone; Group 4, controls. After 24 mo., Groups 1 and 2 showed hyperplastic changes in and steadily increasing wt. (20-30 x normal wt.) of thyroids, as well as increased heart wt.; tumor incidence was 60% and 15%, resp.; latent periods were 9 and 14 mo., resp. Histologic examination revealed no cell malignancies. In Groups 1 and 2 there were the following benign tumor types (number): papillary (9 and 2); follicular (2 and 1); solid (1 and 0), resp. No tumors nor abnormal wt. gain were seen in Groups 3 and 4.

64-505 A STUDY OF THE CARCINOGENIC ACTION OF URETHAN IN MICE. (It.) Della Porta, G. (Dept. Exptl. Biol., Natl. Inst. Study Cure Cancer, Milan, Italy), J. Capitano, W. Montipò and L. Parmi. Tumori 49(6):413-427, 1963.

Results previously reported in CRA 1(7):#1289,

1963 are confirmed in experiments carried out with a larger number of CTM albino mice and with a different dose schedule of urethan (U). In addition, the authors have investigated the carcinogenic effects of U admin. at birth (1 or 3 mg s.c.) and found no significant difference in the incidence and latency of lymphosarcomas as compared with young adults. Results as regards reticulosarcoma were questionable. The incidence of hepatomas, however, was much higher (33.3% in females and 70.9% in males) in groups treated at birth than in older animals (1.3% and 5.9%, resp.); in controls hepatomas were found in 4.5% males and in none of the females. The reverse was true for mammary tumors (only 3 mammary carcinomas and 2 sarcomas were found among 57 females treated at birth); controls and animals treated at wk. 5 showed the same incidence, but the latency periods were shorter in the latter group. Lung adenomas were found in 42-84% of all animals treated and only in 7% of male and 2% of female controls. Controls showed a higher percentage of hepatic angiomas and orbital gland tumors.

64-506 TRENDS IN CARCINOGENESIS BY URETHAN ADMINISTRATION TO NEW-BORN MICE OF DIFFERENT STRAINS. (E.) Trainin, N. (NCI, Bethesda), A. Precerutti and L. W. Law. Nature (London) 202:305-306, 1964.

C3Hf/Lw, DBAf or BALB/c newborn (24-hr. old) mice were treated with a single dose of urethan (U; 0.05 ml of 4% soln. in distilled water s.c. = 2 mg) and 1 yr. later at autopsy no U-induced leukemias or lymphomas were seen. However, the incidence (number of tumors/number of mice) of hepatomas, liver hemangiomas and lung adenomas as well as the percentage of animals with tumors at autopsy was: female BALB/c mice, 0/20, 3/20 (15%) and 97/20 (90%); male BALB/c mice, 0/15, 1/15 (6%) and 50/15 (63%); female DBAf mice, 0/16, 26/16 (81%) and 5/16 (25%); male DBAf mice, 30/15 (86%), 0/15 and 11/15 (43%); female C3Hf/Lw mice, 158/14 (100%), 0/14 and 3/14 (21%); male C3Hf/Lw mice, 261/15 (100%), 0/15 and 2/15 (13%), resp. The BALB/c mice were in poor physical condition with dyspnea due to the massive lung involvement at the time of sacrifice.

64-507 COMPARATIVE STUDIES ON THE INDUCTION OF MAMMARY CARCINOMAS IN WISTAR AND SPRAGUE-DAWLEY RATS BY ORAL ADMINISTRATION OF METHYLCHOLANTHRENE. (Ger.) Engelbart, K. (Farbwerke Hoechst AG, Frankfurt/M., Germany) and D. Gericke. Zschr. Krebsforsch. 66(1):59-64, 1964.

Groups of 50 Wistar and Sprague-Dawley rats were admin. methylcholanthrene (in sesame oil; 10 mg 2-3x/wk., total dose 200 mg, intragastric) for 10 and 12 wk., resp. After 21 wk. tumor rate in survivors was, resp., 35% of 37 and 89% of 28; latent periods were 12 and 10 wk. No invasive

growth or metastases were observed. In the Sprague-Dawley strain, the tumors were predominantly adenocarcinomas, while the Wistar strain showed a greater variety of tumors, ranging from solid carcinomas to squamous cell epitheliomas. Attempts to induce mammary carcinomas with a single oral dose of 100 mg failed; only 26% of the Sprague-Dawley and none of the Wistar rats developed tumors with 21 wk.

64-508 PROCEEDINGS OF THE GERMAN CANCER CONGRESS, MAINZ, SEPT. 26-28, 1963. (Ger.) Marquardt, S. Med. Klin. 59(9):358-361, 1964.

The main topics were: (1) Leukemias and reticulos, (2) Experimental and clinical fundamental research and pathogenesis of cancer, and (3) Sociological and legal problems concerning cancer pts. Topic (1) included a discussion of agents capable of inducing leukemia: ionizing radiation, anthracene and benzene derivatives, endogenous metabolites such as indole and indican, viruses, and hereditary factors were mentioned. Under topic (2), the concept of syncarcinogenesis was discussed; it was found that simultaneous admin. of 2 carcinogens reduced the latent period and the dosage required to produce tumors. The carcinogenic effect of total body irradiation was analyzed. Topic (3) was concerned mainly with the probability of traumatic induction of cancer. A comprehensive study of nevus cell nevi showed that, in spite of traumatic damage, no melanomas developed in 380 cases; with respect to insurance claims, the carcinogenic effect of trauma was generally considered negligible.

64-509 TRANSPLANTATION OF SPONTANEOUSLY OCCURRING AND CHEMICALLY INDUCED LYMPHOID TUMORS IN XENOPUS LAEVIS. (E.) Balls, M. (Sta. Exptl. Zool., U. Geneva, Switzerland). Cancer Res. 24(1):44-51, 1964.

Homotransplant in the anuran amphibian Xenopus laevis laevis of spontaneous or methylcholanthrene-induced lymphosarcomas gave positive results in 88 of 93 cases (80 dorsal lymph sac, 10 abdominal cavity and 3 s.c. transplants). Of these, 76 had persistent tumors at the implantation site and 70 developed visceral tumors, predominantly in the liver, kidney and spleen. The possible origin of visceral tumors from implanted tumor cells (metastasis) or host cells (host cell transformation) is discussed.

64-510 CARCINOGENESIS AND INHIBITION OF THE WALKER 256 TUMOR IN THE RAT BY TRANS-4-ACETYLAMINOSTILBENE, ITS N-HYDROXY METABOLITE, AND RELATED COMPOUNDS. (E.) Anderson, R. A. (McArdle Mem. Lab., U. Wisconsin Sch. Med., Madison), M. Enomoto, E. C. Miller and J. A. Miller. Cancer Res. 24(1):128-143, 1964.

The carcinogenic affect of 4-acetylaminostilbene

(AAS), 4-aminostilbene (AS) and their urinary metabolite N-hydroxy-4-acetylaminostilbene (N-OH-AAS) was studied in weanling female (50-60 g), young male and female (100 g) and young adult male (210-240 g) albino rats following i.p. (suspension in soln. of 1.75% gum acacia in 0.9% NaCl; total doses 1.6-28 mg/rat; 3 inj./wk.), s.c. (5.3 μ moles of compound = 1.25 mg AAS in 0.2 ml tricaprillin/rat/inj./wk.) or p.o. admin. The compounds tested were equally carcinogenic in the ear duct gland, but N-OH-AAS was a stronger carcinogen than AAS or AS in the mammary gland, forestomach, s.c. tissue and small intestine and exhibited considerably greater inhibitory action on the growth of the Walker 256 tumor in the rat, while the o-hydroxy metabolite, 3-hydroxy-AAS, had no effect on this tumor. In no case was N-OH-AAS less active than either AAS or AS. Data suggested that N-OH-AAS is one of the proximate carcinogenic metabolites in carcinogenesis by AS. The weak carcinogen, N-hydroxy-4-acetylaminobenzyl had greater carcinogenic activity than 4-acetylaminobenzyl toward the mammary gland of the rat.

4-511 STUDIES ON THE POSSIBLE CARCINOGENICITY OF A POLYGLYCEROL ESTER. (Ger.) Michel, J. (Inst. Gen. Pathol., U. Aarhus, Denmark), A. J. Therkelsen and A. Stenderup. *Erzheimittelforschung* 14(3):238-239, 1964.

The polyglycerol ester "P.A.F.", marketed by emulsion A/S, Palsgaard, Denmark, as an emulsifier, was admin. orally to 175 male and female C57BL/6J strain mice at a dosage of 100 g/10 kg of diet. Littermates of the treated mice were used as controls. After 15 1/2 mo., the rate of mammary adenocarcinomas and of leukemias (which is relatively high in this strain) was the same for controls and treated animals. Weight curves and survival rates showed no significant differences.

4-512 HEXOKINASE ACTIVITY IN HOMOGENATES OF NORMAL, REGENERATING, AND PRECANCEROUS LIVER AS WELL AS IN PRIMARY AND TRANSPLANTED HEPATOMAS. (Ger.) Sydow, G. (Inst. Exptl. Cancer Res., German Acad. Sci. Berlin, Berlin-Charité). *Acta Biol. Med. German.* 12(4):517-518, 1964.

Hepatomas induced by admin. of diethylnitrosamine (DEN), 0.25 mg/day in 10 ml water, to a total of 100 mg, showed increased hexokinase activity as compared to normal livers. The following mean

values of hexokinase activity, expressed as μ g glucose utilization/mg N/10 min., were found: normal liver, 28 ± 4 ; regenerating liver, 16 ± 2 ; precancerous liver after DENA, 67 ± 12 ; primary DENA-hepatoma, 42 ± 8 ; transplanted DENA-hepatoma, 20th passage, 288 ± 8 . The marked difference between hexokinase activity of primary and transplanted hepatomas is attributed to their different degrees of malignancy.

64-513 SERUM RIBONUCLEASE DURING THE PROCESS OF DAB CARCINOGENESIS AND TUMOR GROWTH. (E.) Zytko, J. (Montreal Cancer Inst. Res. Lab., Canada) and A. Cantero. *Canad. J. Biochem.* 41(12):2391-2396, 1963.

A low-protein, basal diet containing 0.06% of dimethylaminoazobenzene (DAB) was fed to male Wistar rats (180-230 g), while serum RNase (blood obtained by cardiac puncture) was determined weekly. The activity of this enzyme was diminished 50-60% by wk. 3 and remained low throughout the testing period (32 wk.). The size of DAB-induced tumors had no bearing on serum RNase activity. Blood samples were also taken from a second series where Sprague-Dawley rats had been inj. s.c. with 0.5 ml of Novikoff hepatoma (ascites form; approx. 1.68×10^8 cells). Supernatants of ascitic fluid collected 6-7 days after inoc. were used for analysis of RNase. A slight increase in serum RNase on days 2 and 7 after inoc. was seen in 3/4 rats, but a sufficient number was not tested to draw a conclusion. The ascites fluid was found to contain an appreciable amount of RNase, yet the washed tumor cells contained only 7-8% of that found in normal liver homogenates.

64-514 STUDIES ON THE EFFECT OF 3-METHYL-3,4-DIHYDROXY-4-PHENYL-BUTYNE-1 (SUBSTANCE Ko 339) ON CHICK EMBRYOS. (Ger.) Wurmbach, H. (Inst. Zool., U. Bonn, Germany). *Aerzt. Forsch.* 17(7):383-391, 1963.

The agent, which is used clinically as a mild sedative and hypnotic, showed no teratogenic effect when inj. into the air chamber of chick embryos at normal dosage on days 2-8 after start of incub. Admin. after completed development of the allantochorion produced local hemorrhages. Higher doses and inj. into the yolk increased the rate of mortality and induced embryo deformities. The deformities encountered were similar to those observed in the controls due to nutritional deficiencies of the hens. Histological studies of various organs showed no significant abnormalities.

See also abstract nos.: 401,403,409,415,444

VIRAL CARCINOGENESIS

- 64-515 GROWTH OF LEUKEMIA VIRUS IN VIVO. (Jap.)
Nishira, Y. (Dept. Path., Nara Coll.
Med., Japan). Nippon Rinsho (Jap. J. Clin. Med.)
21(11):2377-2379, 1963.

When newborn mice were inoc. with Moloney leukemia virus, the incidence of leukemia was 48% and av. killing days (KD) was 233 days. After serial passage in mice with 25 mg of virus homogenates (after centrifugation at 30,000 g) av. KD became shortened up to 74 days through 3 passages but plateaued thereafter. No correlation was found between incidence or latent period and age of mice used (up to 8 days) or sex. When groups of mice were inoc. with tumor from mice that died on days 59, 72 and 93, av. KD were 157, 100 and 88, resp.; the incidences of leukemia were 14%, 75% and 88%, resp. This indicates that virus activity was higher in the mice whose tumors developed later and survived longer. Reciprocal interference between mammary tumor virus and Moloney leukemia virus, with the production of each tumor, was also observed.

- 64-516 TUMOR INDUCED BY ADENOVIRUS 12. (Jap.)
Yabe, Y. (Dept. Microbiol., Okayama U.,
Japan). Nippon Rinsho (Jap. J. Clin. Med.)
21(11):2383, 1963.

When adenovirus Type 12 (A-12; standard strain Huie) was inoc. into the lungs of newborn hamsters, lung sarcomas developed in 8/10 after 33-99 days. No tumors developed after inoc. of Types 2, 3, 7, 7a, 9, 10, 11 and 14. The A-12-induced tumor was serially transplantable in newborn hamsters with increasing tumor takes. In tests with inactivated A-12-infected tissue cultures, there appeared to be no contamination with polyoma virus or SV40. The carcinogenic activity of A-12 was neutralized by antibody against A-12 in human serum.

- 64-517 FORMATION OF DELAYED TUMOURS IN HAMSTERS
INOCULATED WITH ROUS VIRUS AFTER BIRTH
AND FINDING OF INFECTIOUS ROUS VIRUS IN INDUCED
TUMOUR P₁. (E.) Svoboda, J. (Inst. Exptl. Biol.
Genet., Czech. Acad. Sci., Prague) and V. Klement.
Folia Biol. (Praha) 9(6):403-411, 1963.

A continuation of a previous study abstracted as CRA 1(8):#1547, 1963 on Rous sarcoma (RSV) virus-induced tumors in Syrian hamsters. After inoc. of hamsters with 2.0 ml of a 50% suspension of RSV (Prague strain), early tumors were followed by delayed tumors (fibro- and polymorphocellular sarcomas) in 4/6 survivors after a latent period of about 6 mo. Successive passages with one of the tumors (P₁) were successful in 100% of 5-day-old hamsters but in only a few adult hamsters. Crude P₁ tumor (5 x 10⁵ cells) extract induced sarcomas in 3/4 of inoc. chicks and 1.0 ml and 1.5 ml inoc. of cell-free filtrate induced tumors in 4/4 chicks in both cases. After approx. 1 yr.

of observation, no tumors or other specific pathology were noted in hamsters inoc. with purified RSV on the first day after birth.

- 64-518 COMPARISON ON THE BIOLOGICAL PROPERTIES
OF TUMOURS FORMED IN RATS AFTER THE AD-
MINISTRATION OF TWO VARIANTS OF ROUS SARCOMA. (E.)
Klement, V. (Inst. Exptl. Biol. Genet., Czech.
Acad. Sci., Prague), P. Chýle and J. Svoboda.
Folia Biol. (Praha) 9(6):412-419, 1963.

Tumors and hemorrhagic cysts were observed by the fourth wk. in 28 rats (age 24 hr.) inoc. s.c. with 0.3 ml of 50% Rous sarcoma suspension (Schmidt-Ruppin variant). Tumors, mostly fibrosarcomas with some signs of polymorphocellular transition, were seen in 50% of the rats. Tissue suspension (50%) of 4 of these tumors (designated S₁, S₂, S₃ and S₄) when inoc. into White Leghorn chicks (age 1-3 wk.) resulted in 1/1 tumors from S₁; 0/2, 2/2, 0/3 tumors from S₂; 1/1 and 1/3 tumors with S₃; 0/1, 2/3, 2/3, 2/2 tumors with S₄. The most active tumor was S₄, giving greater numbers of tumors and even when cell suspensions (instead of tissue suspensions) were employed; inoc. of S₄ cell-free culture fluids and cell-free filtrates of centrifugated conc. induced no tumors. Admin. of Schmidt-Ruppin and Prague strains of Rous sarcoma virus showed analogous interaction mechanisms, but marked differences in percentage of incidence and in latent periods of the tumors induced. (See CRA 2(1):#517, 1964.)

- 64-519 BIOLOGIC PROPERTIES OF THE FOWL TUMOR
VIRUS B77. (Cz.) Thurzo, V. (Oncol.
Inst. Bratislava, Czech.), J. Smida, V. Smidová
and D. Šimkovič. Bratisl. Lek. Listy
43(12) (Part 2):697-701, 1963.

See CRA 1(5):#907, 1963.

- 64-520 ELECTRON MICROSCOPIC STRUCTURE OF MYXOMA
VIRUS AND SOME REACTIVABLE DERIVATIVES.
(E.) Padgett, B. L. (Dept. Med. Microbiol.,
U. Wisconsin, Madison), M. J. Wright, A. Jayne and
D. L. Walker. J. Bact. 87(2):454-460, 1964.

Electron microscope studies using the phosphotungstic acid (PTA) negative staining technic revealed 2 general types of particles in preparations of myxoma virus (Moses strain) grown in rabbit kidney cells in tissue culture. The majority of the particles were rounded or rectangular with av. lengths and widths of 296 and 254 mμ, resp., and with convoluted surfaces composed of complex arrangements of tubular elements. Some particles were surrounded by membranes. A second form (10% of the virus population) showed more rectangular particles with wavy or scalloped margins and measured 325 x 278 mμ. These had closely fitting membranes, finely granular surfaces and internal

parallel projections. Reactivable virus particles prepared by treatment with heat showed very little alterations in gross appearance, whereas those treated with urea and sodium dodecyl sulfate showed irregular edges, greatly altered tubular structures and permeability to PTA.

64-521 THE INFLUENCE OF p-AMINOSALICYLATE, AS USED IN NUCLEIC ACID ISOLATION, ON THE LACTIC DEHYDROGENASE ACTIVATING VIRUS IN THE MOUSE TUMOR, SARCOMA I. (Ger.) Georgii, A. (Dept. Path., U. Munich, Germany), P. Goldbrunner and D. Brdiczka. *Naturwissenschaften* 51(3):66, 1964.

A virus-like agent present in mouse Sarcoma I, which previously had been found to produce a marked increase in serum lactic dehydrogenase (LDH) of inoc. mice, was not demonstrable in RNA, DNA, or RNA/DNA preparations isolated from the sarcoma with the aid of p-aminosalicylate (PAS). More detailed studies showed that PAS homogenization at 37°C inactivated the LDH-activating agent within 15 min. This inactivation was not prevented by nuclease inhibitors such as bentonite. Injection of purified PAS homogenates into newborn mice also failed to produce the LDH effect. It is assumed that the enzyme-activating effect of the LDH-agent depends on an intact protein-nucleic acid complex.

64-522 CYTOPHOTOMETRIC MEASUREMENTS OF DNA CONTENT OF MONKEY KIDNEY CELL CULTURES AFTER INFECTION WITH ADENOVIRUS TYPE 3. (Ger.) Jeffer, G. (Dept. Pathol., Justus-Liebig U., Giessen, Germany) and W. Sandritter. *Zschr. Naturforsch.* (B) 19b(2):134-136, 1964.

Infection of monkey kidney tissue cultures with the Type 3 adenovirus resulted in the appearance of intranuclear inclusion bodies which may be small (1-2 μ) and granular, honeycomb-like, or large single granules with sharp borders. The nuclei with inclusion bodies were not different in size from those without them, but their DNA content was higher by from 1-2 times to as much as 10 times. However, there is no difference in the DNA conc. among nuclei with different types of inclusion bodies. The different forms of inclusion bodies were interpreted as being developmental stages of viruses. This is borne out by the fact that before infection, tritiated thymine is incorporated only into the periphery of the nucleus, while after infection, it was found in the inclusion bodies. Studies with P^{32} uptake showed that at the time the inclusion bodies became visible, no more P^{32} was taken up, indicating that the appearance of these bodies represents the completion of viral synthesis.

64-523 BUOYANT DENSITY OF FRIEND LEUKEMIA VIRUS. (E., Abstract) Stim, T. B. (Roswell Park Mem. Inst., Buffalo, N. Y.), F. C.

Wissler and J. T. Grace, Jr. *Clin. Res.* 12(2):288, 1964.

In view of the different symptoms that follow in mice after infection with Friend leukemia virus, an investigation was made of possible viral heterogeneity in the virus inoculum. Upon analysis by isopycnic centrifugation in CsS at 5°C, density of the virus ranged between 1.203-1.208 g/ml. Hence there did not appear to be any viral heterogeneity in the virus inoculum.

64-524 OXIDASE-POSITIVE PARAMYELOBLASTOMA IN THE SO-CALLED LYMPHOMA SYNDROME IN AFRICAN CHILDREN. (E.) Hasselmann, C. M. (U. Clin. Skin Venereal Dis., Erlangen, Germany). *Derm. Trop.* 2(4):207-210, 1964.

After reviewing (28 references) the incidence, pathology and distribution of this "so-called" lymphoma, the author adds support to the myelogenic hypothesis of the pathogenesis of these tumors by reporting the first finding of an oxidase-positive paramyeloblastoma among such tumors in an ovarian metastasis found in a 9-year-old girl from Kampala, Uganda.

64-525 A POSSIBLE MECHANISM FOR THE PRODUCTION OF VIRUS-INDUCED TUMOR. STUDIES ON PROLIFERATION OF CELLS INFECTED WITH POXVIRUS. (Jap.) Kato, S. (Res. Inst. Microbiol. Dis., Osaka U., Japan). *Nippon Rinsho* (Jap. J. Clin. Med.) 21(11):2380-2383, 1963.

Utilization of H^3 -thymidine to study the process of its incorporation into cowpox virus infected cells (cells were exposed to H^3 -thymidine, 5 μ C/ml, for a period of 2 hr.) revealed that in such cells B-inclusion bodies are produced in parallel with the synthesis of DNA in the cytoplasm. Furthermore, comparison of the extent of DNA synthesis in the nuclei of B-inclusion-body bearing cells (by cowpox virus), noninclusion-body bearing cells and control cells showed that the DNA synthesis in the nuclei of the B-inclusion-body bearing cells was markedly inhibited. This inhibition of DNA synthesis in the nuclei of such cells was also proven by a markedly decreased number of silver grains per labeled nucleus. These cells with a poor nuclear DNA production are known to undergo degenerative cellular destruction. In order to explain the mechanism of cell proliferation by poxvirus, it was suggested that some cell-growth promoting factor might be produced from virus cell complexes undergoing such a degenerative process.

64-526 IDENTIFICATION AND QUANTITATIVE DETERMINATION OF MYELOID CHLOROLEUKAEMIA VIRUS WITH THE AID OF THE RESISTANCE PHENOMENON. (E.) Prigogina, E. L. (Inst. Exptl. Clin. Oncol., USSR Acad. Med. Sci., Moscow) and A. A. Stavrovskaja. *Nature* (London) 201:934-936, 1964.

A group of 2-month-old mice twice immunized (with a 2-wk. interval) with a 10% myeloid chloroleukemia virus (MCLV)-induced leukemic tissue extract showed high resistance against the inoc. of established strains (LZ, L-309, LBI; LD₅₀ of >10⁴-10⁸ cells) originally induced by MCLV, while control animals died from leukemia after inoc of 10²-10³ leukemic cells (LD₅₀ of <10² or 10³ cells). Resistance also developed in animals immunized with the supernatant of spleen monolayers of animals with MCLV-induced leukemia. MCLV-induced LZ strain was transplanted into animals infected with different viruses and resistance was observed both after MCLV inoc. and after infection by Moloney's and Masurenko's virus. Lack of resistance was seen in animals immunized by Gross-virus-induced leukemic tissue extract of AKR mice and against LZ cells in animals treated with spontaneous mammary tumor or healthy spleen-liver extracts of Strain A female mice. The NK/Ly lymphoma did not grow in MCLV infected mice after inoc. of 10⁴ cells, while in untreated animals the LD₅₀ was <10³. Antigens related to, or identical with, antigens induced by MCLV were detected not only in leukemia strains originally induced by the same virus but in the cells of NK/Ly lymphoma. Pretreatment by MCLV had no effect on the transplantability of Ehrlich tumor and mammary carcinoma of A-OMG mice. MCLV-titration by its resistance-inducing (RI) capacity showed that virus preparations contained 10^{4.6} and >10^{6.0} RI Dose₅₀/0.2 ml.

- 64-527 SOME PROPERTIES OF BOVINE PAPILLOMA VIRUS. (E.) Boiron, M. (Leukemia Res. Inst., St.-Louis Hosp., Paris), J. P. Levy, M. Thomas, J. C. Friedmann and J. Bernard. *Nature (London)* 201:423-424, 1964.

In a paper devoted largely to previously described work, it is mentioned that C57BL mice and rats developed no tumors when inj. with bovine papilloma virus (in contrast with C3H/EB mice and golden hamsters). (See also CRA 1(11): #1982 and *ibid.*, #1983, 1964.)

- 64-528 INDUCTION OF RESISTANCE AGAINST ISO-TRANSPLANTATION OF VIRUS-INDUCED MYELOID LEUKAEMIAS. (E.) Pasternak, G. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin-Buch) and A. Graffi. *Brit. J. Cancer* 17(3):532-539, 1963.

Inbred mice (Strains CBA, C57B1, XVII and AKR) were used as experimental animals and tumor donors (inj. with cell-free filtrates of virus-induced leukemias) to reveal if they possess a specific antigenicity. For immunization, several treatments were conducted: s.c. inj. 2 or 3 times at 2-wk. intervals, of 0.2-0.3 ml of irradiated leukemic tissue (1:4 soln.) to isologous recipients; similar inj. to homologous recipients but with non-irradiated tissue suspension; and inj. s.c. with subthreshold cell doses to isologous

recipients. Lymph nodes and spleens from animals with leukemias L1061 and L1937 were used for transplants to homologous recipients; L1205 was used, in addition, with the isologous recipients. Resistance was found against grafts of virus-induced myeloid leukemias by the pretreatment with isologous tumor material (78.9%; controls 12.0%). Resistance was also induced against isologous grafts by pretreatment with homologous grafts of myeloid leukemia (63.7%; controls 33.3%), but pretreatment of these with homologous grafts of spontaneous lymphatic leukemia (AKR strain) provided no resistance (1.9%; controls 7.1%). It is concluded that the cells of the 2 types of leukemias contain different antigens. (See also CRA 1(12): #2122, 1964.)

- 64-529 INTERACTION BETWEEN POLYOMA VIRUS AND DIFFERENT TISSUES OF MOUSE AND HAMSTER *IN VITRO*. (E.) Diderholm, H. (Inst. Virol., U. Uppsala, Sweden) and T. Wesslén. *Arch. Ges. Virusforsch.* 14(1):45-54, 1963.

The reaction of polyoma virus (T and SE strains) with various tissue homogenates of adult and newborn mouse strains (C57 Black, A.Ca and N.M.R.I.) and golden hamster was studied. Highest inhibition titers (IT; expressed as reciprocal of highest dilution) for the newborn mouse were obtained with salivary gland (SG), brain (B) and kidney (K) homogenates (8192, 1024 and 512, resp.); low IT (64-256) were seen for lung (L), intestine (I), liver (LI) and heart (H); there was no inhibition with skin (S) or thymus (T). IT in the adult mouse were similar, except for homogenates of SG, S and T (1024, 32 and 16, resp.). In newborn hamsters, highest IT were seen for B and SG homogenates (1024 and 512, resp.); lowest IT for LI, H, I and T; no inhibition for S. In adult hamsters, highest IT were seen for homogenates of B (2048) and SG, K and L (512 each). Homogenate inhibition was slightly greater than that of intact cells. The greatest inhibition seen was in the microsomal fraction (the cell sap was also effective). Periodate and receptor destroying enzyme (RDE) were found to reduce the inhibitory effect, whereas trypsin, chymotrypsin, lipase, ether, chloroform and Tween 80 did not. A correlation is suggested between the inhibitory capacity of tissue and its susceptibility to virus infection.

- 64-530 INFECTION OF NATURALLY INSUSCEPTIBLE CELLS WITH DNA OF POLYOMA AND SV40 VIRUSES. (E.) Diderholm, H. (Inst. Virol., U. Uppsala, Sweden) and T. Wesslén. *Acta Path. Microbiol. Scand.* 59(2):271-272, 1963.

Phenol extracts of virus suspensions of polyoma virus (P; 2048-16,384 HA units/0.5 ml) grown in mouse embryo cultures and SV40 virus (10^{8.5}-9.7 TCID₅₀/ml) grown in kidney cells of the African green monkey were found to produce cytopathic changes (prevented by the addition of antisera)

mouse embryo, monkey, swine and calf kidney cultures identical with those caused by the intact virus. Monkey, swine and calf cell cultures were found to be naturally insusceptible to P virus; mouse, swine and calf cells to SV40. The infectious properties of the extracts were inhibited by DNase but not by RNase.

- 531 THE HISTOGENESIS OF GROSS'S VIRAL INDUCED MOUSE LEUKEMIA. (E.) Goodman, B. (Dept. Med., U. Colorado Med. Ctr., Denver) and M. H. Block. Cancer Res. 23(10):1634-1640, 1963.

The histogenesis of mouse leukemia was studied in C3H(f)Bi mice (8-12 days old) receiving i.p. inj. of thawed cell-free extract (C3HG9; prepared according to Gross's method from the liver, spleen and thymus of 2 mice with lymphosarcoma confined to the thymus). Of 58 animals (sacrificed between 18-153 days after the inj.), 20 showed a definite abnormality of one or both lobes of the thymus: cortical atrophy in 1 or 2 lobes was noted in 9/20; regeneration in 10/20; lymphosarcoma *in situ* (no thymic capsule or other organ invasion) in one thymic lobe in 4/20; lymphosarcoma in 6/20 (2/6 with local invasion of the capsule; 4/6 with invasion by lymphosarcoma cells of distant organs, such as lungs, liver, kidney, ovary, small intestine, lymph nodes, spleen and marrow) at the time of sacrifice. Two of the 20 showed leukemic involvement of the peripheral blood and 1/20 showed evidence of generalized sarcomatous involvement of a tracheal node. No examples of early bone marrow involvement were seen. The histogenesis of Gross leukemia in the C3H(f)/Bi mouse closely resembled that of certain other forms of mouse leukemia.

- 64-532 VIRUS-LIKE PARTICLES IN THE CELLS OF LYMPHOMA 6C3HED. (E.) Sobin, L. H. (New York Hosp.-Cornell Med. Ctr., New York). Cancer Res. 24(1):64-69, 1964.

Spherical, virus-like particles 60-100 m μ in diameter, found in the cytoplasm of cells of lymphoma 6C3HED obtained from solid s.c. and ascites tumors in C3H mice and from *in vitro* suspensions and having a dense, double, outer shell and a more lucent core, are described. These particles, which, when formed, are seen only within the confines of the cisternae, arise at the membranes of the endoplasmic reticulum by a budding process, show no association with the Golgi apparatus, or the central or peripheral cytoplasm. Cells from ascitic fluid and tissue culture contained more of these particles than did cells from solid s.c. tumors. The morphology of the particles conform with Bernhard's Type A virus, which has been found in a variety of spontaneous and induced, transmissible and transplantable murine neoplasms.

- 64-533 LYMPHOMATOSES IN AFRICAN CHILDREN. (Ger.) Daildorf, G. (Sloan-Kettering Inst., New York). Arch. Kinderheilk. 170(1):51-56, 1964.

In Central African children, lymphosarcomas of the maxilla, ovary, or retroperitoneal lymph nodes are relatively frequent, while acute leukemias are rare. This ratio is diametrically opposed to that observed in Europe and the USA. The geographical distribution pattern of the tumors has been found to coincide with that of malaria; a possible interrelationship between the two diseases has been suggested. Investigating the possibility of a viral etiology of the African lymphosarcomas, the author isolated several filtrable viruses of the enterovirus and smallpox type, but identification has not been completed as yet.

See also abstract nos.: 400,406,412,414,416,417,445,478

64-534 STATISTICAL OBSERVATION ON AUTOPSY CASES OF RETICULOSARCOMATOSIS. (Jap.)

Matumoto, A. (Dept. Otorhinolaryng., Fac. Med., U. Kyoto, Japan), K. Makimoto, R. Uno, M. Sakamoto, M. Tamura and N. Ibara. Jibiinkoka Rinsho (Otorhinolaryng. Clin.) 56(1):33-37, 1963.

Among 16,782 autopsies performed in Japan from 1958-1960, there were 215 cases of reticulum cell sarcoma. Among 74 of these cases in which the initial clinical site was known, age distribution was between 7-80 with about 70% in those between 30-69. In 42 cases the initial tumor was found during otolaryngological examination; however, there was no correlation between tumors of this area and the extensions found at autopsy. Tumor extension to the lung and kidney was frequently observed at autopsy although these sites were rarely involved initially. Initial tumors not in the areas of the ear and larynx tended to metastasize more frequently to lymph nodes of the retroperitoneal and mesenteric regions.

64-535 RELATIONSHIP OF BLOOD GROUP SUBSTANCES AND SECRETION SUBSTANCES IN CERTAIN BENIGN AND MALIGNANT DISEASES OF THE STOMACH AND DUODENUM. (Cz.) Bártová, A. (1st Clin. Int. Med., Palackeho U. Sch. Med., Olomouc, Czech.), J. Burián and K. Bárta. Vnitřní Lek. 9(9): 864-868, 1963.

Blood groups among 1001 pts. with stomach carcinoma were as follows: O--27%; A--47.5%; B--16.6% and AB--8.9%. Normal values for the local district and for all of Czechoslovakia were, resp.: 34% and 31.5%; 36% and 42%; 19.9% and 17.3%; 8.9% and 9.1%. In an analysis of those with resectable and non-resectable carcinomas, the number of pts. and percentage of total within each group was, resp.: O--107, 42.9% and 142, 57.1%; A--193, 44.8% and 238, 55.2%; B--70, 45.1% and 85, 54.9%; AB--45, 50.5% and 44, 50.0%. Among 77 pts. with stomach carcinoma, distribution of secretors and nonsecretors was, resp.: O--17 and 4; A--29 and 15; B--8 and 3; AB--1 and 0; for this group as a whole there was, thus, the usual distribution (about 75% and 25%). Among 28 pts. with stomach ulcers and 32 pts. with duodenal ulcers there were 13 and 18 nonsecretors, resp.

64-536 STATISTICAL INVESTIGATION OF THE RELATIONSHIP BETWEEN BLOOD GROUPS A, B, O AND CANCER. (It.) Cavalli, A. (Inst. Oncol., Turin, Italy), C. Corradi and P. Calderini. Minerva Med. 55(11):326-329, 1964.

Blood group distribution was studied in a total of 2,171 pts. of both sexes with various types of cancer (uterus, stomach, breast, lungs and bronchi, large bowel, prostate) which were seen in the Institute of Oncology of Turin and in the Dept. of Medical Pathology of the U. of Turin

during the yr. 1953-1963, and in a group of 2,360 control subjects. Results (percent; pts. and controls) were: Group O, 38.88 and 44.74; Group A, 47.90 and 41.15; Group B, 10.83 and 10.00; Group AB, 2.39 and 4.11. Statistical analysis showed that the differences between the O and A Groups were highly significant. When the blood group distribution was calculated separately for each type of cancer, the results were in general like those of the general cancer population with the exception of mammary carcinoma, where the blood group distribution was the same as in noncancerous subjects.

64-537 LEUKEMIA AND IONIZING RADIATIONS. (Cz.) Libánský, J. (Inst. Hemat. Blood Transfus., Prague, Czech.). Vnitřní Lek. 9(7): 628-637, 1963.

In a review of the literature (51 references), despite the fact that acute irradiation with high doses and chronic irradiation with small doses appear to be contributory to the development of hemoblastoses, the author found no such connection in 110 of his own cases. Mortality due to leukemia and other malignant blood diseases appears to be increasing in Czechoslovakia. Mortality due to leukemia in 1948 and 1960 was, resp., 390 and 743. Mortality in 1949 and 1960 was, resp.: for Hodgkin's disease, 167 and 380; for lymphosarcoma, 81 and 239; for myeloma, 18 and 112.

64-538 OCCUPATIONAL TUMORS OF THE BLADDER. (CLINICAL CONTRIBUTION.) (It.) Coppola, R. (Civil Hosp., Caserta, Italy) and R. Montanaro. Rass. Int. Clin. Ter. 43(22): 1230-1239, 1963.

In a review (14 references) of occupationally-induced cancers, the authors report the case of a 68-year-old retired man who developed a papillomatous carcinoma of the bladder, occluding one ureter, after 18 yr. of employment in a dye works in which he was constantly in contact with benzidine.

64-539 CONTRIBUTION TO THE STUDY OF THE EPIDEMIOLOGY OF CARCINOMA OF FEMALE GENITAL ORGANS. (Ser.) Milošević, B. (Inst. Epidemiol., Belgrade, Yugoslavia), E. Stolević, B. Milojčić, S. Krajinovic, S. Udicki, R. Cvetkovic, M. Obradović, M. Nastasović, R. Novčić and S. Sokić. Med. Glas. 17(11-12):445-447, 1963.

In a study of 100 pts. with carcinoma of the cervix uteri and 35 with other genital carcinomas (uterus, ovary, vulva, tube) the highest incidences were found in the age group 46-50 yr. (25.0% and 23.5%, resp.). In the group as a whole 30% were nulliparous or had aborted; about 30% had cancer in the family. Sexual life began at

ages up to 21 yr. for 53% while 3% were virgins. Abstention during menses was observed by 46.2% and about 30% practiced temporary or prolonged abstinence. As to partners, 56.7% had one, 23.8% had 2 and 16.4% had 3 or more. The hygiene of the partners was considered good in 62.6% of the cases and poor in 34.3%. Contraceptives were used by 3% of the females and 15% of the males. Irrigation with chamomile was used by 13% while in single cases vinegar, sage, etc., were employed. While there was some variation, the pts. had about the same socioeconomic and educational background.

540 ETIOLOGY AND DEVELOPMENT OF CARCINOMA OF THE CERVIX UTERI. (Ger.) Hillemanns, G. (U. Freiburg i. Br., Germany), E. Grundmann and K. Rha. *Bibl. Gynaec., Fasc. 29*. S. Karger, Basel, 224 pp., 1964.

A detailed review of clinical and histologic findings in 1942 pts. with carcinoma of the cervix uteri (including material from conizations, curettages, and biopsies), the authors report that cervical tumefaction appears to begin with the development of 1 or more foci of multicellular, precancerous changes in tissue of the vulva, portio uteri, or endocervix (most frequently, the portio), which eventually begin to spread as an intraepithelial invasion of atypically proliferating cells, frequently moving out from more than one center simultaneously over a "latency period" of 1-5 yr. Such multicentric cancerization was demonstrable in 1/5 pts. studied; occurrence of more than 1 type of tumor in the same pt. was frequent. Contributory or precipitating factors included chronic inflammation (especially during pregnancy); cyclic menstrual changes; chronic irritation due to sexual activity or resulting from abortion or childbirth; and other sources of stimulation of the area, which interfere with the maturation of the pavement epithelium. Among 21 pts. with carcinomas of the portio uteri, the first evidence of a cancerous tendency appeared to be a change of ploidy in the cells of unstable irritated epithelial tissue, accompanied by increased protein synthesis. An abrupt reduction of ploidy to normal values preceded the beginning of neoplastic growth and intraepithelial invasion, which first involved diploid basal cells. (In basal cell carcinomas, the cancerous cells remained diploid; in most carcinomas of the cervix portio uteri however, they became tetraploid.) Increased proliferation was accompanied by a significant increase of total nucleic acids, and an increased RNA:DNA ratio. Reduction of ploidy was accompanied by a marked reduction of cytoplasm and a proportional increase of nuclear vol.; both changes were maximal when the pt. developed a surface carcinoma, and approx. 3 as great when she developed an invasive carcinoma. In pavement epithelial tissue derived from the normal portio uteri an organ-specific antigen (AG) was demonstrated in mitochondria and chromosomes, which was related to an antigen found in human mesenchymal tissue but not to that found

in the epithelial tissues of the human kidney. AG was severely reduced in pavement epithelial tissue in pts. with surface carcinomas of the portio uteri, and was completely lacking in pts. who developed invasive carcinomas of the same site. The reduction of AG content took place gradually, during the period of precancerous tissue changes, and appeared to be due to plasmagenic (rather than mutagenic) intracellular changes. With the beginning of infiltrative tumor growth, indications of the presence of a cancer-specific form of AG were seen for the first time. The authors conclude that carcinogenesis begins with potentially reversible, protein determined, structural changes in the cell (including increased nuclear vol. with increase of basic nucleohistone); these, in turn, precede the chromosomal changes which make the cell susceptible to endogenous and/or exogenous carcinogenic influences. In carcinoma of the cervix uteri, for example, actual carcinogenesis is preceded by the presence of multiple foci of abnormal pavement epithelium and a gradual increase of such abnormal tissue precedes the (frequently sudden) onset of intraepithelial proliferation and subsequent, large scale conversion of abnormal to actively malignant cells. Although conversion of abnormal to malignant cells can also be demonstrated in very small, isolated groups of cells within the preinvasive, abnormal epithelial tissue, these are "contained" in the form of microtumors; the authors emphasize the fact that the stage of intraepithelial proliferation is a forerunner of cancerization as such, rather than a cancerous process in itself.

64-541 GYNECOLOGIC SARCOMAS OF WOMEN IN EL SALVADOR. (Sp.) Diaz-Bazan, N. (Dept. Obstet. Gynec., U. El Salvador Sch. Med., San Salvador) and R. Masferrer. *Arch. Col. Med. El Salvador* 16(4):229-256, 1963.

In the Republic of El Salvador gynecologic cancers represent 46.4% of all neoplastic diseases and 67.3% of cancer in women. Statistics from the country's largest general hospital (Hospital Rosales) show that from 1950-1962 there was a total of 3,253 cases of malignant gynecologic cancer; 42 (1.4%) were sarcomas and 3,211 were carcinomas. The number of pts. with sarcomas/carcinomas by site was: uterine cervix, 13/2,870; uterine body, 18/112; ovary, 7/109; vagina, 2/60; vulva, 2/58; tubes, 0/2. The 42 cases of gynecologic sarcoma are analyzed and the world literature related to its distribution by site is briefly reviewed (107 references). Among the 31 pts. with sarcoma of the uterine body or cervix, 21 (70%) were less than 50 yr. of age; the remainder were 50-85 yr. of age. A case of sarcoma of the uterine body was found in a pt. who had received 15 yr. previously radiation therapy for a uterine fibromyoma. The two vulvar sarcomas were a fibrosarcoma and a reticulum cell sarcoma in pts. 75 and 56 yrs. of age resp.; the latter pt. had multiple metastases of uncommon localization (lungs, kidneys, thyroid, pancreas, and 4th dorsal vertebra). Primary

sarcoma of the tubes was not observed but the authors report to have observed a rare case of metastatic sarcoma of the tubes in a pt. who had previously undergone subtotal hysterectomy for a cervical sarcoma.

- 64-542 CONCERNING THE GENETIC RELATIONSHIP BETWEEN SARCOIDOSIS (BENIGN LYMPHO-GRANULOMATOSIS; BESNIER-BOECK-SCHAUMANN'S DISEASE) AND MALIGNANT LYMPHOGANULOMATOSIS (HODGKIN'S DISEASE). (Ger.) Jörgensen, G. (Inst. Human Genet., U. Göttingen, Germany). *Deutsch. Arch. Klin. Med.* 209(3):307-330, 1964.

A study of the family histories of 2,471 pts. with sarcoidosis showed that in 3 cases one parent had died of histologically confirmed Hodgkin's disease; in a fourth case, two siblings had Boeck's sarcoidosis while a paternal cousin had died of Hodgkin's disease. This is considered insufficient evidence of a genetic relationship between the two diseases; however, the relatively high familial incidence of each disease alone, as shown by a survey of the literature, suggests the presence of some hereditary factor.

- 64-543 CONTRIBUTION TO THE ETIOLOGY OF BRONCHIAL CARCINOMA. EVALUATION OF 1000 PERSONAL CASES. (Ger.) Wachsmuth, W. (Surg. Clin., U. Würzburg, Germany) and H.-J. Viereck. *Deutsch. Med. Wschr.* 89(13):606-611, 1964.

A statistical evaluation was made of questionnaires sent to 1000 pts. with bronchial carcinoma. The male:female ratio was 16:1; the most frequently affected age group was that from 50 to 60 yr. (48.6%). A history of smoking was given by 91.4%. In 524 histologically diagnosed cases, squamous cell carcinomas constituted 57.1%; oat cell carcinomas 27.3%. Both types had increased several-fold in recent yr., while the incidence of adenocarcinoma had remained constant (5.3%). Analysis of the occupational distribution showed that persons working in restaurants (exposure to tobacco smoke) were most frequently affected; in second place were those exposed to exhaust fumes (truck drivers, policemen, road construction workers). Least frequently affected were persons in the health services. The incidence of bronchial carcinoma in urban areas was higher than in rural regions.

- 64-544 CARDIOVASCULAR DISORDERS AND TUMORS IN RELATION TO THE TOTAL INCIDENCE OF ILLNESSES. (Sw.) Wijkström, S. *Kvart. Svenska Nat.-Foren. Hjärt-o. Lungsjuk.* 59(1):8-16, 1964.

See CRA 1(12):#2207, 1964.

- 64-545 STATISTICAL OBSERVATIONS ON THE INCIDENCE OF LARYNGEAL CANCER IN RELATION TO AGE. (It.) Giaccai, F. (Dept. Otorhinolaryng.,

U. Florence). *Boll. Mal. Orecch.* 81(5):554-564, 1963.

Between 1947-1963, the E. N. T. Dept. of the U. of Florence treated 825 cases of laryngeal cancer (770 men, 55 women). Of these pts., 85.2% were 40-69 yr. of age; 10.3% were above 69 yr. and 4.5% were below 40. When incidence was studied in terms of age-corrected figures in 5-yr. cohorts, the max. percentage frequency was in individuals of age 60-64. These figures may be considered as representative of the national incidence since the author's series comprised pts. from many Italian provinces and various professional categories. More women than men were observed in the youngest and in the oldest age groups.

- 64-546 ENDOMETRIAL HISTOPATHOLOGIC CHANGES IN MALIGNANT TUMORS OF THE OVARY. (It.) Cimellaro, M. (Dept. Obstet. Gynec., U. Rome), F. Pietropaolo and G. Memmi. *Clin. Obstet. Gynec.* 65(10):518-529, 1964.

Cystic glandular hyperplasia of the endometrium was observed in 5 pts. (4/5 48-65 yr. old, 1/5 36 yr. old) in association with malignant tumors of the ovary. Endometrial hyperplasia of a typical type was seen in 2 pts., while in another it was polypoid in form and was accompanied by manifestations of senile cystic atrophy; in a third pt. it was preceded by other hyperplastic disturbances (cervical polyps) and in a fourth it assumed atypical aspects which were on the borderline of malignancy. It is concluded that in the presence of an ovarian tumor, cystic glandular hyperplasia of the endometrium should be considered as a precancerous condition, even in those cases where it assumes typical histologic aspects. In disagreement with general findings of endometrial hyperplasia in association with endocrine tumors of the ovary, the authors have observed one case in which a granulosa cell tumor was associated with endometrial atrophy.

- 64-547 NOSOGRAPHIC CHARACTERISTICS OF LARYNGEAL CANCER IN WOMEN. (It.) Celestino, D. (Dept. Otorhinolaryng., U. Rome) and G. De Rosa. *Boll. Mal. Orecch.* 81(5):459-474, 1963.

The analysis of 640 cases of laryngeal cancer in men and 99 (69 personal, 30 from the literature) in women showed that the median age of appearance of this condition was the same for both sexes (55 yr.). Distribution (percentage) in age groups for men and women was, resp.: 30-40, 5.07 and 9.09; 40-50, 23.1 and 26.22; 50-60, 43.03 and 31.31; 60-70, 24.02 and 24.24; 70-80, 3.06 and 8.08; 80-90, 0.04 and 1.01. The differences between the sexes in the age groups from 50 to 80 yr. are statistically significant. The incidence of circumscribed cancer of the vocal cords among men and women was similar (19.2% and 21.7%, resp.) while that of the vestibule was found in 35.4% males compared to 15.9% of the females. Metastases from the

latter site were seen in only 2/11 female pts. while they were seen in 50% of the male pts. In a study of possible predisposing factors, prior inflammatory conditions were seen in 4/15 vocal cord cancers; a history of syphilis was found in 5/69 (still active in 3 at time of hospitalization). Among those with syphilis was 1 of 2 with metastases from the vestibule. Among 5 with prior surgery (uterus 4, mammary adenoma 1), 4 developed cancer of the vocal cord. Among 69 pts. 11 (16%) were smokers; 8 of these were heavy smokers. In agreement with recent findings in male pts. (see CRA 1(11):#2011, 1964) preferential localizations among the smokers were the vestibule and epiglottis. A relationship is thus suggested between the lower frequency of vestibular cancer and the lower percentage of smokers among women.

64-548 MORBIDITY, MORBIDITY RATE AND MORTALITY FROM LEUKEMIA IN POLAND FROM 1951-1959. REPORT I. MORBIDITY. (Pol.) Janicki, K. (3rd Clin. Int. Dis., Acad. Med., Cracow, Poland). Pol. Tyg. Lek. 19(18):663-666, 1964.

According to data obtained by the Ministry of Health, the incidence of leukemia in Poland appeared to increase steadily during most of the period studied. The total number of hospitalized and registered cases and the rate per 10,000 of population were, resp.: for 1951, 757 and 0.3; for 1958, 1,258 and 0.43; for 1959, 1,056 and 0.36. For the same 3 yr., these data for males were: 412 and 0.34; 660 and 0.47; 592 and 0.42. For females results were: 345 and 0.26; 598 and 0.40; 464 and 0.30. The author suggests that the statistically significant increase in morbidity may be due in part, but not entirely, to better diagnosis and improved public health programs. (See also CRA 2(2):#374, 1964.)

64-549 THE ASSOCIATION OF HEPATIC CIRRHOSIS WITH PRIMARY AND SECONDARY TUMORS OF THE LIVER. (Fr., Abstract) Van der Vekens, P. Lyon Med. 210(48):1151, 1963.

Among 4,946 autopsies performed at the University of Ghent during the yr. 1948-1963, primary cancer of the liver was found in 20 (0.44%); 16 hepatomas, 3 cholangiomas, 1 mixed type); extrahepatic metastases were seen in 8/20 (40%). Hepatic cirrhosis was found in 14/20 (70%). During the same period the author also observed 165 cases of hepatic cirrhosis of which 14 (8.4%) had primary cancer of the liver. The association of the two conditions occurred most frequently in men. Primary cancer of the liver without cirrhosis showed the same frequency in both sexes. Secondary cancer of the liver was very rarely seen among cirrhotic pts.

64-550 Ii BLOOD GROUP AND DISEASE. (E., Abstract) Schmidt, P. J. (NCI, Bethesda), M. H. McGinniss and P. P. Carbone. Clin. Res. 12(2):288, 1964.

Weak or absent I antigen was found in 20/116 pts., including 7/11 with acute leukemia, 1/2 with chronic lymphocytic leukemia and 7/23 with chronic myelogenous leukemia. In the last group of pts. there was no relationship between lack of I and treatment, white cell count or the Philadelphia chromosome abnormality. Other negative I pts. had cervical carcinoma, neuroblastoma, lupus or mitral stenosis. Positive I pts. were found in all of these disease categories. Since 99.9% of normal adults are known to be I positive, the authors believe they have demonstrated that I antigen sites may be lost or blocked as a result of disease processes, rather than being related to genetic factors.

64-551 MASS SURVEY FOR THE CANCER OF CERVIX UTERI IN CHINA. A PRELIMINARY REPORT. (E.) Lim, Kha-Ti (Chinese Acad. Med. Sci., Peking), Kao, Jun-Chuan, Chang, Chih-Fen and Chen, Pen-Chen. Sante Publique 6(2):163-173, 1963.

A more detailed account of CRA 1(12):#2174, 1964.

64-552 CARCINOMA OF THE CERVIX IN ISRAEL. (Heb.) Ratzkowski, E. (Dept. Oncol., Hadassah U. Hosp., Jerusalem), A. Hochman and J. Amir. Harefuah 49:187-190, 1964.

Among 311 pts. with carcinoma of the cervix seen at Hadassah Hospital (which treated virtually all such cases in Israel) between 1933-1957, 194 were Jews (74 of oriental, 110 of occidental and 10 of unknown origin). The incidence of the disease was highest at age 45-54 and did not differ in the 2 ethnic groups. A difference in health education was observed: 50% of those of Oriental origin came for treatment late, at Stages III and IV. Of the total, 12.8% were diagnosed at Stage I. While 12.8% of all pts. were childless, this total was 22.7% in those of occidental origin; however, there was no change in the incidence. In 1960-1961 in Israel the number of new cases reported was 2.25/100,000 women. Treatment was external irradiation with intravaginal and intracervical radium applications.

64-553 ON BILHARZIASIS AND MALE BREAST CANCER IN EGYPT: A PRELIMINARY REPORT AND REVIEW OF THE LITERATURE. (E.) El-Gazayerli, M. M. (Dept. Surg., U. Alexandria, Egypt) and A.-S. Abdel-Aziz. Brit. J. Cancer 17(4):566-571, 1963.

Of 224 biopsies of breast malignancies seen between 1950-1959, 219 were carcinomas and 5 were of sarcomas (all in females); of the 219 pts. with carcinoma, 6.4% (14 cases) occurred in males (in other countries, the max. was 1.3% in men). Of the 14 men with breast carcinoma, 7 showed a history of or the presence of bilharzial infection and 3 additional pts. with breast cancer showed a strongly positive reaction to bilharzial antigen. Gynecomastia was seen in 8 pts. who showed marked

liver disturbances from the bilharzial process. The ratio of males to females with breast cancer in this series was 14 to 204. Though the occurrence of bilharziasis among the male breast cancer pts. may be accidental, the authors suggest that the high percentage of breast cancer in men consistently observed in Egyptian figures is attributed to hyperestrogenism secondary to bilharzial liver fibrosis which may be a causal factor in men with breast cancer.

- 64-554 LYMPHOMA IN AFRICA. (E.) Davies, J. N. P. (Albany Coll. Med., N. Y.). New Eng. J. Med. 270(7):374-375, 1964.

In a letter to the editor, the possible etiology of lymphoma in Africa is discussed in relation to previously published reports. The standardized cancer rates per 100,000 for 0-4-year-old males and females and 5-14-year-old males and females in various countries were, resp.: Kyadondo region of Uganda, 9, 5 and 12, 8; Johannesburg, 10, 7 and 10, 7; Norway, 16, 16 and 10, 9; U. S. whites, 23, 21 and 15, 14; U. S. nonwhites, 22, 12 and 13, 7. Statistically African lymphoma might be regarded as the biologic equivalent of lymphatic leukemia elsewhere but bone marrow studies did not suggest that this was a form of leukemia. Evidence for "infectivity" (possibly by a virus carried by an insect vector) would include altitude as a limiting factor (unlike leukemia) and in some areas the disease was focally distributed with limited evidence of focal epidemics and seasonal distribution.

- 64-555 THE RELATION BETWEEN GEOGRAPHICAL VARIATION OF HEALTHINESS AND THE MAIN CAUSES OF DEATH. I. THE CORRELATION BETWEEN EXPECTATION OF LIFE AT BIRTH AND STANDARDIZED DEATH RATES OF THE MAIN CAUSES OF DEATH. (E.) Shigematsu, T. (Dept. Public Health, Kyushu U. Sch. Med., Fukuoka, Japan) and T. Hirohata. Kyushu J. Med. Sci. 14(1):39-53, 1963.

In Japan during 1947-1955, the standardized death rates from malignant neoplasm scarcely influenced the geographical variation of expectation of life at birth. It was thought this may be because regional differences in this disease are smaller than that from other causes and are less influenced by natural and social factors. For males in 1950 the highest standardized death rate/100,000 from malignant neoplasm was 128.3 in the prefecture of Nara and the lowest rate was 61.1 in Iwate; similar rates for females were, resp., 87.9 (Nara) and 60.8 (Iwate). In 1955 the highest and lowest death rates for neoplasms for men were, resp., 123.5 (Yamagata) and 73.1 (Kagoshima); similar rates for women were 86.6 (Niigata) and 58.5 (Kagoshima).

- 64-556 MULTIPLE, PRIMARY MALIGNANT TUMOR: DOUBLE CARCINOMA. (Jap.) Yamashita, H.

(Dept. Radiol., Hosp. Cancer Res. Inst., Japan), S. Amino, M. Gomi, R. Matsuoka and Y. Kuroda. Rinsho Hoshasen (Clin. Radiol.) 8(11):797-806, 1963.

Of 36 cases with multiple primary malignant tumors (27 proven histologically, 9 clinically) seen from 1946-1960, 6 were concurrent (3 male, 3 female) and 30 (24 male, 6 female) were non-concurrent. The interval between appearance of the primary and secondary carcinoma was approx. 3.4-4.4 yr.; most occurred within 2 yr. As to age, 31/36 (86%) were over 50 (av. 59.3). As to site, most concurrent double carcinomas were in the stomach. In the non-concurrent double carcinomas primary sites, in order from the most to least frequent were: pharynx, maxillae and oral cavity; the secondary tumor was frequently in the g.i. tract. Organs involved with multiple tumors were: large intestine (5.8%), pharynx (1.7%), thyroid (1.6%), upper jaw (1.4%), stomach (1.3%), rectum (1.2%), skin (1.2%).

- 64-557 END RESULTS OF MALIGNANT TUMORS OF THE TESTIS. (E.) Magnus, K. (Cancer Registry, Montebello, Norway). Acta Un. Int. Cancr. 19(6-7):1461-1464, 1963.

Statistics on 1702 histologically confirmed cases of malignant tumor (seminoma, teratoma, other or unspecified) of the testis from 6 sources (Finland, England and Wales, Norway, U. S. Centralized Registries, U. S. Connecticut and U. S. Teaching Hospitals) were reported. The age distribution (<35-45 yr.) was similar for all the sources except Finland where the highest proportion of pts. was in the oldest age group 45 or more yr.), despite a relatively young population. The proportion of seminomas was higher and that of the teratomas was lower in Europe than in the USA, but this may be due to differences in pathological classification. More than 90% of the cases were given surgical or combined surgical-radiological treatment; the latter was more common in England and Norway than in the U. S.

- 64-558 CARCINOMA OF THE COLON IN ULCERATIVE COLITIS. (E.) Goldgraber, M. B. (Dept. Med., U. Chicago Sch. Med., Ill.) and J. B. Kirsner. Cancer 17(5):657-665, 1964.

Cancer of the large bowel has developed thus far in 33 of approx. 1,200 pts. with chronic ulcerative colitis under prolonged observation at the University of Chicago. Cancer in these pts. occurred approx. 20 yr. earlier than in those with the usual cancer of the bowel; in most cases it arose after an av. of 17 yr. after start of symptoms. The lesions were distributed more uniformly throughout the large bowel than were those of the usual cancer and were multifocal in origin. While the risk of colonic cancer appeared greater among pts. with ulcerative colitis that began at an age below 13 yr., the duration of the colitis until recognition of the cancer was not shorter

in this group than among older pts. In an earlier series of pts. colonic carcinoma was the cause of death in 14/86 pts. with chronic ulcerative colitis at the time of death as contrasted to a normal expectance of fatal colonic or rectal carcinoma in 1.9/86 persons of comparable age, sex and race.

- 64-559 RESULTS OF TREATMENT OF 2000 CONSECUTIVE CASES OF GASTRIC CARCINOMA. (E.)
Bucalossi, P. (Natl. Inst. for the Study and Treatment of Tumors, Milan, Italy), U. Veronesi and F. Lomonaco. *Acta Un. Int. Cancr.* 19(6-7): 1502-1505, 1963.

The present study evaluates the results of treatment of 2000 cases of gastric carcinoma at the Cancer Institute of Milan from June 1928 to December 1961. Of the cases reported, 1,365 were males and 635 were females; range of ages was 15-85 with highest frequencies between 55-59 yr. for males and 60-64 yr. for females. There was previous history of gastric ulcer in 101 pts. and of duodenal ulcer in 21, indicating a positive correlation only between gastric ulcer and gastric cancer. A comparison of cigarette smoking in approx. 1,327 male gastric cancer pts. and in 1000 male controls showed that 31.3 and 22.1%, resp., were heavy smokers (>20 cigarettes/day); 23.6 and 24.2%, resp., were moderate smokers (10-20 cigarettes/day); 27.5 and 30.4%, resp., were mild smokers (<10 cigarettes/day); 17.6 and 23.3%, resp., were nonsmokers. Among male pts., as compared to 1000 male controls, 54% vs. 48%, resp., consumed more than 1 liter/day of wine; 26.8% vs. 19%, resp., consumed more than 2 liters. Among women pts., consumption of wine did not differ from that of the general population. No conclusions were drawn with respect to either smoking or consumption of alcoholic beverages as possible contributory or etiologic factors in gastric cancer.

- 64-560 PRIMARY CANCER OF THE LIVER. (E.)
Mogena, H. G. and J. M. Aroca Ruiz-Funés. *Bull. Inst. Med. Res. Univ. Madrid* 16(1):15-40, 1963.

In 28/7,270 autopsies at the Medical School and Provincial Hospital of Madrid and in 36/60,726 pts. necropsied or biopsied at the Clinic of Internal Medicine, primary cancer of the liver was found. In this series, 9 secondary liver cancers were found for each case of primary cancer. Primary liver cancers usually occurred between 40-60 yr. of age; 69.25% were males. Cholangioma was more frequent in women. The authors discuss various possible predisposing or etiologic factors, such as estrogen level, unbalanced diet, fats; viral hepatitis, cirrhosis, parasitosis and hydatid cyst. The two histologic forms encountered were hepatoma (78%) and cholangioma (22%). Clinical symptoms, liver function studies, auxiliary diagnostic methods and therapy

are also discussed. There is an extensive review of the literature (141 references).

- 64-561 VARIATION IN LEUKAEMIA INCIDENCE. (E.)
Lanzkowsky, P. (Dept. Child Health, U. Capetown, S. Africa). *Brit. Med. J.* 1:910, 1964.

Of 40 Capetown, South African children (6 wk.-13 yr.) with acute leukemia, incidence as to type was 27 lymphoblastic, 8 myeloblastic, and 5 stem-cell or unspecified. As to origin, 24/40 cases were white (12 from Capetown itself, 12 from country areas), 16/40 cases were Cape colored (13 from Capetown, 3 from country areas), and 0/40 were African (Bantu). Clinical onset during the winter mo., June-August, was reported for 15/40 (37.5%; lymphoblastic 10, myeloblastic 3, other types 2). Onset between September-November was seen in 8/15 (20%; lymphoblastic 6, myeloblastic 1, others 1); between December-February, 9/40 (22.5%; lymphoblastic 5, myeloblastic 2, others 2); and between March-May, 8/40 (20%; lymphoblastic 6, myeloblastic 2). The author feels that this seasonal variation may shed some light on a possible pathogenic mechanism in this disease.

- 64-562 THE MALIGNANT TRANSFORMATION OF FIBROUS DYSPLASIA. (E.) Schwartz, D. T.
(Presbyterian Hosp., New York) and M. Alpert. *Am. J. Med. Sci.* 247(1):1-20, 1964.

A critical analysis is presented of 28 cases where fibrous dysplasia (FD) was transformed to sarcoma (26 cases from world literature (91 references), 2 from records of the Presbyterian Hosp.). The incidence of such malignant degeneration is estimated at 1:200, the malignant change being more frequent in males. Sarcomas occurred more often in polyostotic than in monostotic FD. Mean age of onset of sarcoma was 32 yr., with a mean lag of 13.5 yr. after onset of FD. Most common site of these sarcomas was the cranio-facial region, most common histologic type osteogenic sarcoma. Important symptoms of malignant transformation were pain, swelling, and a significant change in the X-ray picture. In 16/28 cases the pts. received no irradiation. Among the 12 who were irradiated, only 5 were considered to have received a dose sufficient to have possibly contributed to the development of the sarcoma. No normal bones developed sarcoma, only those with FD.

- 64-563 CAUSE OF DEATH IN LEPROSY PATIENTS-MORTALITY DUE TO MALIGNANT TUMORS. (Jap.) Ri, T. (Natl. Tama Res. Inst. Japan), T. Maruyama, N. Sasaki and K. Fukushi. *Nippon Byorigaku-kai Kaishi (Trans. Soc. Path. Jap.)* 52:195-196, 1963.

In autopsies of leprosy pts. performed between 1953-1960, malignant tumors appeared to be the

cause of death in 21/114 (18.4%); prior to 1937 this figure was 1.5%.

- 64-564 CLINICAL AND ETIOLOGICAL ASPECTS OF BONE SARCOMAS. (Ger., Abstract)
Ehlers, P. N. and G. Ott. Zbl. Chir. 89(10): 348-349, 1964.

An analysis is presented of 780 cases of parosteal, osteogenic, and myelogenous sarcomas. About 50% of them originate in the knee region; in contrast to carcinoma, their incidence shows no increase with advanced age (this explains the widely divergent incidence in various populations, i.e., through differences in life expectancy). Bony sarcomas tend to appear at an earlier age; many are induced by professional hazards (work with phosphorus in the watch industry). Skeletal sarcomas through irradiation are sometimes seen after the use of the drug Peteosthor (Th-X) or exposure to strontium 89 and 90, which accumulates in bones, especially in children. Trauma may induce them, especially after nail fixation, or wiring of bones. A fibro-osteoid sarcoma was also found in the region of an old bone homotransplant. Early symptoms are few (17% of all cases seen for the first time are already metastatic), but the prognosis after surgical therapy is not unfavorable. A 5-year-survival of 31.9% can be obtained. (See also CRA 1(12):#2044, 1964.)

- 64-565 THE STATUS OF THE OVARY IN CANCER OF THE ENDOMETRIUM. (Sp.) Nogales, F. (2nd Clin. Fac. Med., U. Madrid, Spain) and M. del Carmen Tornero. Acta Oncol. (Madrid) 1(2):364-375, 1962.

In a contribution to the controversial question of the possible endocrine origin of endometrial carcinoma, the authors investigate the anatomic pathology and the function (vaginal cytology and excretion of urinary estrogen) of the ovary in 110 cases of endometrial carcinoma, 20% of which were premenopausal and 80% postmenopausal. A persisting increased estrogenic activity was

found in the group of postmenopausal pts. However, the evidence was inconclusive as to chronic hyperestrogenism being the causal agent of uterine adenocarcinoma, since no significant differences were seen in the estrogen activity compared to normal women of the same age. The ovaries were not responsible for the postmenopausal secretion of estrogens; cytological findings were similar to those found in normal women of the same age. Thecomas were seen in 3/88 postmenopausal pts. and granulosa cell tumor in 1/88.

- 64-566 RADIOPHOTOGRAPHIC CASE FINDING OF BRONCHIAL CANCER. ILLUSION OR ACTUAL POSSIBILITY? (Fr.) Pache, L. (Clin. Therap., Canton Hosp., Geneva, Switzerland). Rev. Med. Suisse Rom. 84(2):100-125, 1964.

In an extensive review (43 references) of clinical and pathologic aspects, diagnostic problems and therapy of bronchial carcinoma, the author reports that in the canton of Vaud in Switzerland the radiophotographic general screening of 440,000 people (1954-1961) for possible tuberculous infections led to a definite diagnosis of bronchial carcinoma in 24 cases. They were all men and their age ranged from 49 to 85 yr. (15/24 in the age group 49-69 yr.). The incidence of bronchial carcinoma and active tuberculosis for each 10,000 people examined was, resp., 0.5 and 10.

- 64-567 HODGKIN'S DISEASE WITH SIMILAR CLINICAL MANIFESTATIONS IN IDENTICAL TWINS. (Sp.) Dutrey, J. An. Cat. Pat. Tuberc. (B. Air.) 20:202-204, 1964.

Reported is the case of identical male twins who developed Hodgkin's disease in the cervical lymph nodes and died 2 yr. after the onset of the condition. In one the disease occurred at the age of 25 yr. and in the other at 38 yr. A review of the related literature (12 references) reveals the rarity of the phenomenon: only 7 other cases have been reported since 1903. These findings support the theory of a genetically determined predisposition to the development of Hodgkin's disease.

See also abstract nos.: 410,411,466,483

MISCELLANEOUS

- 64-568 RESISTANCE TO TUMOR TRANSPLANTATION INDUCED BY RIBOSOMES. (Fr.) Lacour, F. (Lab. Immunol., Inst. Gustave Roussy, Villejuif/Seine, France), É. Nahon and C. Verger. *C. R. Acad. Sci.* 257(16):2357-2359, 1963.

Immunization of male and female Swiss mice with total doses of 4 mg ribosomes (RNA/protein = 1), followed 2 wk. later by i.p. inj. of 4×10^3 VP ascites cells, showed that when the ribosomes were derived from ascitic cells only 2/18 died with ascites, as opposed to 9/19 receiving ribosome from normal embryonal cells and 15/21 unimmunized animals. The difference between Group 1 and either 2 or 3 was statistically highly significant while that between Groups 2 and 3 was not.

- 64-569 TUMOUR CELLS IN CHAMBERS IMPLANTED INTO IMMUNIZED RATS. (E.) Teichmann, B. (Robert-Rössle Clin., German Acad. Sci. Berlin) and G. Wittig. *Nature (London)* 200:373, 1963.

A group of 30 rats were subjected to two transplantations of Walker carcinoma tissue 16 days apart with excision of the tumors after 8 days; 3 and 4 rats after the transplantations, resp., relapsed and were discarded. Sixteen days after a third transplantation (and 51 days after the first), 21/23 rats showed no sign of tumor growth. Diffusion chambers containing Walker carcinoma tissue were implanted i.p. into the 21 rats. Upon removal 5 wk. later, survival and growth of the tumor cells could be demonstrated in all chambers by histological and biological methods.

- 64-570 ANIMAL EXPERIMENTAL STUDIES OF THE RELATIONSHIP BETWEEN WOUND HEALING AND TUMOR GROWTH WITH PARTICULAR ATTENTION TO CLINICAL SEQUELAE. (Ger.) Baron, H. *Langenbeck Arch. Klin. Chir.* 304:712-721, 1963.

In white Wistar rats, i.m. inoc. with 0.2-0.3 ml Walker carcinoma cell suspensions of 1:1 in physiologic saline after 1-3 stressings by exposure to a temperature of 130° for 30 min. (or by heat + mechanical wounding) resulted in 27.2% tumor deaths as compared to 35.6% among unstressed controls. In animals stressed twice, at an interval of 8 days prior to inoc., tumor deaths were reduced to 23.4%; in animals stressed twice, at an interval of 14 days, they were reduced to 8.6%; and in animals stressed repeatedly at irregular intervals, they were 9.4%. Statistically significant inhibition of tumor growth was not seen in animals stressed only once or in animals inoc. prior to completion of wound-healing. The author speculates that blood from persons who have sustained repeated accidents or undergone repeated surgery may contain defense elements which would be of benefit to cancer pts.

- 64-571 VITAMIN C AND CANCER. (Ger.) Schmidt, F. (Inst. Exptl. Oncol. Res., German Acad. Sci. Berlin, Potsdam-Rehbrücke, Germany), H. Schmandke and B. Gassmann. *Zschr. Aertztl. Fortbild. (Berlin)* 57(23):1315-1324, 1964.

Total vitamin C content, L-ascorbic acid, and dehydroascorbic acid were determined in the tumor tissue and parenchymatous organs of 57 rats bearing various transplanted tumors in various stages of development. The total vitamin C content of the tumor tissues was significantly higher than that of liver, brain, testes, and spleen, which in turn was lower than that found in the corresponding organs of 7 controls. Yoshida sarcoma, Walker carcinosarcoma, and Jensen sarcoma had a significantly higher vitamin C content than the slow-growing Shay chloroma. In ES 4-sarcoma and Yoshida sarcoma, the content increased as the tumor developed ($p < 5\%$). Similar results were found in guinea pigs inoc. with Daels sarcoma; hypervitaminosis C promoted, rather than inhibited, the growth of this tumor. Dehydroascorbic acid was demonstrated in various conc. in all organs examined, as well as in tumor tissue. The conflicting literature on the role of vitamin C in the development and growth of human and animal tumors is also reviewed (196 references).

- 64-572 VITAMIN A-INDUCED CONGENITAL DEFECTS IN HAIRLESS MICE. (E.) Mauer, I. (Neuro-Endocr. Res. Unit, Willowbrook State Sch., Staten Island 14, N. Y.). *Biol. Neonat.* 6(1-2): 26-37, 1964.

- 64-573 BASAL CELL CARCINOMA FOLLOWING BCG VACCINATION. REPORT OF TWO CASES. (E.) Ben-Hur, N. (Rothschild Hadassah U. Hosp., Jerusalem, Israel), J. Avni and Z. Neuman. *Dis. Chest* 44(6):653-655, 1963.

Basal cell carcinoma was found at the site of inj. 5 and 13 yr. following BCG immunization in a man and a woman, ages 40 and 36, resp.

- 64-574 AN EPIDERMOID CARCINOMA DEVELOPING IN A CONGENITAL PULMONARY MALFORMATION. (Fr.) Hertzog, P. (Dept. Anat. Path., Foch Hosp., Suresnes, France), J. Roujeau and J. Marcou. *J. Franc. Med. Chir. Thorac.* 17(1):33-38, 1963.

A 36-year-old woman with a congenital malformation of the lung (an extra-lobular, extra-pleural cul-de-sac communicating with the lower lobe) developed an epidermoid epithelioma *in situ*. It is suggested that since there is a possibility of the malignant evolution of certain malformations, early excision be practiced, despite the rarity of the condition.

- 64-575 EFFECT OF TRICHOMONAS INFECTION ON THE GENESIS OF ATYPICAL EPITHELIUM ON THE VAGINAL PORTION OF THE UTERUS. II. A CLINICAL EVALUATION OF 2650 WOMEN WHO CONSULTED THE CLINIC FOR ONCOLOGIC SCREENING. (Cz.) Zajacova, E. (1st Inst. Obstet. Gynec., Bratislava, Czech.). Bratisl. Lek. Listy 44(1):90-103, 1964.

Among 373 women affected with vaginal trichomoniasis and 2277 without trichomonal colpitis, abnormal epithelium was present in 15.3% and 5.8%; hyperactive epithelium in 3.7% and 0.7%; markedly atypical epithelium in 4.6% and 0.6%; clinically undetectable carcinoma in 1.3% and 0.0%; classical carcinoma in 1.1% and 1.2%; total atypias in 26.0% and 9.2%, resp. Of those with cervixes which showed no inflammation or laceration, only about 11% showed atypias compared to 30.4% in those with cervical lacerations. It was mentioned that chronic inflammation often leads to cervical lacerations. Statistically, a very significant correlation was found between trichomoniasis and the development of atypical epithelium; to a lesser degree, this correlation was also found with cases of hyperactive, and to a still lesser degree with cases of abnormal epithelium of the cervix. No significant correlation between trichomoniasis and clinically undetectable carcinoma or classical carcinoma cases was evident. It was concluded that the infection may be an initial pathogenic factor which triggers the early changes; the later carcinogenic changes may then proceed independently of this factor.

- 64-576 COMPARISON OF NUCLEOLAR EXTRUSIONS IN HUMAN AND ANIMAL NEOPLASMS. (E., Abstract) Duryee, W. R. (George Washington U., Washington, D. C.). Anat. Rec. 148(2): 367-368, 1964.

In a previous report, the author showed that the first detectable change in early human malignancies is increased DNA at the locus of the nucleolar organizer, followed by enlargement of nucleolar RNA, bursting and extrusion into the cytoplasm. In the present study, a comparison of normal and malignant tissues from frogs, salamanders, birds, rodents, and humans showed that increased DNA function of the nucleolar organizer leads not only to localized cytoplasmic growth, but to an increase in the mass of the cell's progeny.

- 64-577 THE INFLUENCE OF SKIN HOMOGRAFTS ON THE DEVELOPMENT OF BROWN-PEARCE CARCINOMA IN RABBITS. (Rus.) Lomakin, M. S. (Inst. Exptl. Biol., Acad. Med. Sci. USSR, Moscow) and E. V. Sokolova. Biull. Eksp. Biol. Med. 57(1):82-85, 1964.

When 15 male chinchilla rabbits received skin homografts 8 days before the intratesticular inoc. of Brown-Pearce carcinoma (0.5 ml of a 20% suspension), there were no takes in 7 and temporary

growth in 8; all eventually became resistant. When tumor inoc. and homografts were done simultaneously, 2/7 were resistant while the others died with tumors on av. day 23. When homografts were made 8 days after tumor inoc. there was intensification of tumor growth and stimulation of metastases in 10/11 (1 was resistant) which resulted in death on av. day 33.5. In untreated controls 4/15 were resistant (2 of these showed temporary tumor growth); 11/15 died with tumors on av. day 31.1.

- 64-578 GENETIC DETERMINATION OF THE TL (THYMUS-LEUKAEMIA) ANTIGEN IN THE MOUSE. (E.) Boyse, E. A. (Sloan-Kettering Inst. Cancer Res., New York), L. J. Old and S. Luehl. Nature (London) 201:779, 1964.

The genetic determination of 197 male and female mice obtained from crosses between C57BL/6(TL-) and A(TL+) strains revealed that the TL+ thymus character in normal A mice behaves as a single dominant gene with its locus in linkage Group IX in close proximity to the D end of the H-2a group of alleles. Perhaps the most outstanding feature of the TL antigen is its appearance in leukemias of strains of mice with a TL- thymus. (See also CRA 2(2):#204 and #205, 1964.)

- 64-579 PRODUCTION OF EMBRYONAL α -GLOBULIN BY TRANSPLANTABLE MOUSE HEPATOMAS. (E.) Abelev, G. I. (Dept. Immun. Oncol., Gamaleya Inst. Epidemiol. Microbiol., Moscow), S. D. Perova, N. I. Khramkova, Z. A. Postnikova and I. S. Irlin. Transplantation 1(2):174-180, 1963.

An α -globulin-related antigenic component was shown to exist in the sera of both embryo and newborn mice, but not in the sera of adult mice; it was also found in the sera of adult mice bearing Hepatoma XXIIa (14-21 days after transplantation) as a result of its synthesis in the tumor tissue and its secretion into the blood. Slight accumulation of the antigen was seen in the sera of mice with slowly growing hepatomas (XXII and XXXVIII) and in the sera of mice with regenerating liver 48 hr. after partial hepatectomy; negative results occurred with 1 hepatoma (XLVI) and 20 different non-hepatic tumors (such as Ehrlich carcinoma, the Crocker and 37 sarcomas, several sarcoma strains induced by methylcholanthrene and benzanthrane, 5 transplantable leukoses, 2 mammary gland tumors, 1 stomach tumor and 2 skin carcinomas). Therefore, the mechanism of its synthesis is present, but repressed, in normal liver cells and its activation in some tumor-bearing animals is caused by the transition of tissue from a resting to a proliferating state. A similar α -globulin was detected in the sera of newborn rats, but not in the sera of adult rats; it also accumulated in the ascitic fluid and sera of adult rats bearing ascitic Zajdela hepatoma.

64-580 COELIAC DISEASE AND MALIGNANT CHANGE.
(E.) Editorial. Lancet 1:544, 1964.

In a discussion on premalignant lesions of the g.i. tract, it was noted that Gough et al. have described 4 pts. with celiac disease who some yr. later (some pts., 20 yr. later) developed reticulum cell sarcomas of the small bowel. When reticulosis occurs (which often appears as a localized and well defined tumor) the best treatment for these pts. is early excision.

64-581 AN UNCOMMON ASSOCIATION: INTRABRONCHIAL SARCOIDOSIS AND HODGKIN'S DISEASE. (Sp.)
Perazzo, D. L. (Dept. Semeiology, U. Buenos Aires), O. R. Pergola and J. E. Duhart. Orientac. Med. 13:62-64, 1964.

Described is the case of a 20-year-old man with sarcoidosis and Hodgkin's disease, both localized intraluminally in the bronchi. The rarity of this localization of either disease suggests that the association in the same pt. may be more than casual.

64-582 A CASE OF PROMYELOCYTIC PARAMYELOBLASTIC ACUTE LEUKEMIA WITH TRISOMIC D AND HAPLOSOMIC C AND G BLOOD CELLS. (Sp.)
Forteza Bover, G. (Dept. Path. Clin. Med. B, Fac. Med., U. Valencia, Spain), R. Baguena Candela, and A. J. Bordon. Med. Esp. 50(297):357-361, 1963.

In a 53-year-old man with acute leukemia the examination of bone marrow cells by the direct technic revealed in all the absence of 2 chromosomes, a small acrocentric of Group G (21-22) and a submetacentric of Group C (6-12), and the presence of an extra chromosome of Group D (13-15). A comparison with related data from the literature shows this to be the third case of trisomy D or haplosomy G in acute leukemia. However, findings are controversial as to the association of acute leukemia with a specific chromosomal aberration.

64-583 A CHROMOSOMAL ABNORMALITY IN A MYELOCYTIC ALEUKAEMIC LEUKAEMIA. (E.)
Makino, S. (Dept. Zool., Hokkaido U., Sapporo, Japan) and M. S. Sasaki. Lancet 1:851-852, 1964.

A female karyotypic abnormality was noted in 22 cells (from a total of the 34 examined with 46 chromosomes) taken from a blood culture of a 43-year-old woman with acute myelocytic leukemia. One of the two X's was replaced by a morphologically abnormal chromosome of medium size with an obscure centromere. The pt. showed no mental or physical abnormalities other than the leukemia. Buccal smears showed a normal female pattern.

64-584 RHEUMATOID ARTHRITIS AND CHRONIC LYMPHOCYTIC LEUKEMIA. STUDY OF TWO CASES WITH AN UNUSUAL ASSOCIATION. (Fr., Abstract)

Kahn, M. F., A. Ryckewaert and J. Welfling. Rev. Rhum. 30(12):801-802, 1964.

Reported are two cases of rheumatoid arthritis in which a chronic lymphocytic leukemia was observed 5 and 15 yr. after the onset of polyarthrititis. In one pt. lymphoid hyperplasia was noted before the appearance of leukemia. This association appears especially interesting in the light of recent findings on the effect of delayed immunity in diseases of the connective tissue and on the role of the lymph glands in the development and pathology of this immunity.

64-585 PEMPHIGOID AND CARCINOMA OF THE PANCREAS. (E.) Boyd, R. V. (U. Coll. Hosp., London). Brit. Med. J. 1:1092, 1964.

A case is reported of a 76-year-old woman, who was blind due to glaucoma, who developed a bulbous eruption (involving the four limbs, back and buccal mucosa), which was diagnosed as dermatitis herpetiformis or pemphigoid, after suffering a pulmonary embolism 4 wk. previously. At necropsy, a carcinoma of the pancreas was found involving the body and tail, without necrosis, and when examined histologically, the pancreatic tumor was a mucus-secreting adenocarcinoma.

64-586 EARLY MOUSE-SKIN RESPONSES TO IRRITANTS. (E., Abstract) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.) and J. R. Baker. Toxic. Appl. Pharmacol. 6(3):350, 1964.

The rapid response (10 min.) in the skin of hairless mice to the application of irritants (such as xylene and croton oil) by the formation of dermal inflammatory exudates containing large numbers of mast cells may be useful in assessing early effects of irritation since the mast cell response lends itself to measurement by cell counts and UV fluorescent methods.

64-587 ACTION OF BILATERAL VAGOTOMY ON THE EXPERIMENTAL NEOPLASTIC LESIONS OF GLANDULAR STOMACH. (E., Abstract) Vilchez, C. A. (Inst. Gen. Exptl. Path., Fac. Med., Natl. U. Cuyo, Mendoza, Argentina) and J. M. Echave Llanos. Naturwissenschaften 51(6):142, 1964.

For an earlier experiment on unilateral vagotomy, see CRA 1(4):#651, 1963. Following bilateral vagotomy, 19 C57L/Mza² 180-day-old female mice received 20-methylcholanthrene (0.3 ml in 0.01 ml aqueous suspension of gum arabic) by inj. into the submucosa of the anterior wall of the glandular stomach. When killed 60 days later, 1 of the animals had a neoplastic lesion limited to the mucosal layer, in 2 the lesions invaded only the submucosa, in 1 the lesion invaded the muscularis propria, 14 had lesions which invaded the peritoneum, and 1 was free of lesions. All the animals had only one tumor, the size of which was greater than those in

the first experiment; however, the histological pattern of these tumors did not differ.

- 64-588 ZINC CONTENT IN GRANULOCYTES OF NORMAL SUBJECTS AND IN PATIENTS WITH CERTAIN HEMATOLOGIC DISEASES. (PRELIMINARY REPORT.) (Pol.) Szmigielski, S. (Clin. Hematol., Inst. Hematol., Warsaw) and J. Litwin. *Pol. Arch. Med. Wewnet.* 34(3):319-321, 1964.

Normal zinc values of granulocytes were determined histochemically in 10 normal subjects and in 42 pts. with various hematologic disorders (14 chronic myeloid leukemia; 8 acute myeloid leukemia; 6 plasmacytoma; 6 osteomyelosclerosis; 4 Hodgkin's disease; 3 chronic lymphatic leukemia; 1 not specified). A decrease in zinc content was found in chronic myeloid leukemia, acute myeloid leukemia, plasmacytoma, and Hodgkin's disease; an increase in zinc content was found in chronic lymphatic leukemia and osteomyelosclerosis.

- 64-589 URINARY CLEARANCE OF 17-KETOSTEROIDS, 17-HYDROXYCORTICOIDS, AND ALDOSTERONE IN POLYCYTHEMIC SUBJECTS. (Hun.) Tényi, I. (Pecs U. Med., Hungary), T. Burger, B. Keszthelyi and M. Németh. *Orv. Hetil.* 104(25):1172-1174, 1963.

The 24-hr. urinary clearance of 17-ketosteroids, 17-hydroxycorticoids and aldosterone was studied in 7 men and 3 women with polycythemia vera and findings were compared to those seen in control groups of 20 normal subjects of each sex, representing the same age groups. Mean values for male pts. were tabulated as follows (mean control values in parentheses): 17-ketosteroids, 15.45 mg (9.2); 17-hydroxycorticoids, 10.7 mg (6.4); aldosterone, 6.32 μ g (7.8). Comparable tabulations for women pts. were 11.3 mg (6.9), 15.48 mg (6.01) and 8.86 μ g (7.6), resp. Previous reports in the literature have indicated means of 10-16 mg/24 hr. for 17-ketosteroid excretion in normal subjects, as contrasted to means of 8-12 obtained in the authors' own clinic over a period of several yr. There were no similar discrepancies with respect to the other 2 substances. Comparable data for pts. with polycythemia vera were not found in literature available to the authors, who conclude that the increase in 17-keto- and hydroxycorticoid steroid levels, as compared to controls, was significant while the difference between aldosterone levels in pts. and controls was not statistically significant. The phenomenon suggests that the neuroendocrine system may play a role in the etiology of polycythemia vera.

- 64-590 STRUCTURAL CHANGES IN HOMOLOGOUS TRANSPLANTS OF A MAMMARY CARCINOMA OCCURRING SPONTANEOUSLY IN A FEMALE NMRI MOUSE. (Ger.) Mohr, H.-J. *Frankfurt Zschr. Path.* 73(1):67-96, 1963.

A spontaneous, cystic, mammary tumor in a female NMRI mouse, homogenized and inj. into the thigh muscles of 12 homologous females, was thus cultivated *in vivo* and similarly transplanted serially through 6 passages. The resulting tumors *in situ* showed progressive structural alterations (histologic and cytologic, but not subcellular) and morphologic changes. Instead of the original loose, large cystic, secretory, partially papillary structure, with little stroma and few mitoses, the first passage yielded a simple, small, tubular adenoma with some adenocarcinomatous characteristics. The tumors of later passages became progressively more solid, with many giant tumor cells, increasingly abundant mitoses and amitoses and a few necroses, developing into full-fledged carcinomas; then finally (passage 6) they became spindle celled, anaplastic, carcinosarcomas, with very many mitoses, chromatin-rich nuclei, and a few giant tumor cells. The cytoplasmic (sub-microscopic) fine structure remained unchanged, but the microscopic nuclear form became variable, with enlarged nuclei, enlarged multiple nucleoli, clumped DNA granules at the wavy nuclear membrane and amitotic nuclear constrictions. Nuclear metabolism appeared to be heightened, with increased synthesis of DNA and RNA. Virus particles were unchanged. The malignant nature of the original tumor appeared to be confirmed by the infiltrative, destructive (necrotizing) nature of subsequent transplants and by the fact of transplantability; however, no metastasis had been demonstrated at the time of report. The progressive de-differentiation observed in succeeding passages was also taken as an evidence of initial malignancy and the morphologic changes, as such, were attributed to selective survival from a heterogeneous cell population (the original tumor) in response to the change of milieu (thigh muscle in place of mammary gland).

- 64-591 COLLAGENOSIS AND HEMOPATHY. (Rus.) Dul'tsin, M. S. (Centl. Inst. Hematol. Blood Transf. (Order "Lenin"), Moscow) and Ia. A. Sigidin. *Ter. Arkh.* 36(1):16-22, 1964.

Myelograms of 100 pts. with various collagenous diseases revealed two deviations from normal. On one hand, WBC was increased in 73/100 (many with simultaneous anemia); in 86/100 there was increase of plasma cells and in 69/100 there was increase of reticular cells. The mechanism of this hematological pathology can be two-fold: (1) the ability of cells to change their structure in the process of collagenous disease, (2) increased capacity of the organism to produce antibodies against their own normal tissues and cells. As any mesenchymal organ, the bone marrow in collagenous disease can be subject to inflammatory and dystrophic changes; these changes together with persistently increased permeability of the bone marrow capillaries appear to be, in some cases, the cause of a pronounced leukemoid reaction down to reactive hemocytoblastosis. Based on this, the authors link collagenosis with leukemias. In support of their belief they

ite 70 other cases of polyarthritis, 2 of which
ave developed acute leukemia during successive
recurrences of arthritis.

4-592 CHROMOSOME STUDIES OF A FROG RENAL
ADENOCARCINOMA LINE CARRIED BY SERIAL
INTRAOCULAR TRANSPLANTATION. (E.) Di Berardino,
A. (Inst. Cancer Res., Philadelphia, Pa.),
J. King and R. G. McKinnell. J. Nat. Cancer
Inst. 31(4):769-789, 1963.

Chromosome analyses were made on spontaneous
primary adenocarcinoma RT-7 of Rana pipiens and
in tumors derived from it serially transplanted
into the anterior chamber of the eye. The line
is essentially diploid; chromosome changes were
seen in only 3% of all tumor cells examined. A
minority of tumor cells (14% of those sampled)
contained nonspecific structural aberrations.
The incidence of stromal cells was very low,
these changes were thus mainly seen in epithelial
cells of the tumor.

4-593 CYTOLOGICAL OBSERVATIONS ON A BOVINE
LYMPHOSARCOMA. (E.) Basrur, P. K.
Div. Anat., Ontario Veterin. Coll., Guelph,
Canada), J. P. W. Gilman and B. J. McSherry.
Nature (London) 201:368-371, 1964.

A 24-hour-old lymph node cell culture from a
Holstein cow with lymphosarcoma showed only 12/64
cells (approx. 18%) carrying 60 chromosomes re-
sembling those of the normal female karyotype
except in 2 autosomes with 25 and 29); there
were also 48 cells in the diploid range, 39 cells
(approx. 61%) carrying 61 chromosomes and 9 cells
(4%) with 62 chromosomes. Only 4 cells were
observed with widely aberrant counts (one with 30,
>100). The distribution of chromosomes in this
culture suggests that the cell type with the
extra sub-metacentric chromosome is mitotically
more efficient than the other cells. The pres-
ence of 2 Barr bodies in 35/50 lymphocytes in the
24-hour-old cultures seemed to indicate that the
extra sub-metacentric is an X chromosome. The
increase in number of 61 chromosome type and the
increase in 60 chromosome type cells in 10-day-
old cultures suggested a 'preference' by culture
environment of normal fibroblast-like cells over
neoplastic cells. Of the 29 cells analyzed from
the 10-day-old cultures, 11 carried the 60 normal
type chromosomes, 3 showed 61 chromosomes, and 17
had numbers from 53-182. It is not known whether
this chromosome trait is characteristic of bovine
lymphosarcoma or that the cell type with the ex-
tra sub-metacentric was the progenitor of the
malignant lymphocytes in the lymph nodes.

4-594 STUDIES OF THE PHILADELPHIA CHROMOSOME.
(E., Abstract) Goh, K. O. and S. N.
Fisher. Ann. Intern. Med. 60(4):729-730, 1964.

The presence of the "Philadelphia" (Ph¹)

chromosome has been demonstrated in the metaphase
nuclei of cells of 20/20 pts. with chronic myelo-
cytic leukemia studied in various stages of the
disease. There was no correlation between number
of positive cells and clinical state of the pt.
This chromosome was not found in 9 pts. with mye-
loid metaplasia nor in the normal identical twin
of a pt. with chronic myeloid leukemia. Higher
percentages were seen in pts. whose leukocytes
were cultured for 48 hr. than in those cultured
for 72 hr. In Ph¹-positive nuclei, the abnormal
chromosomes are usually found adjacent to or close
to a large acrocentric chromosome.

64-595 REFRACTORY ANEMIA, GRANULOCYTIC HYPER-
PLASIA OF BONE MARROW, AND A MISSING
CHROMOSOME IN MARROW CELLS. A NEW CLINICAL SYN-
DROME? (E., Abstract) Freireich, E. J. (NIH,
Bethesda), J. Whang, J. H. Tjio, R. H. Levin,
G. M. Brittin and E. Frei III. Clin. Res. 12(2):
284, 1964.

The author briefly considers the possibility that
the following findings, observed in 3 pts. (classi-
fied cytologically as preleukemic), may represent
a new syndrome: 45 chromosomes, with one of the
6-12 group missing in marrow cells; skin and lym-
phoid cells cytogenetically normal; chronic anemia
and thrombocytopenia; development of a picture
resembling chronic myelogenous leukemia with termi-
nation as acute myelomonocytic leukemia. This
cytogenetic abnormality was not found in over 50
pts. with acute leukemia and in over 70 with chron-
ic myelogenous leukemia.

64-596 STRESS IN THE AETIOLOGY OF BREAST CANCER.
(E.) Lask, M. Med. World (London)
98(3):197-200, 1963.

The author discusses the importance of stress in
the etiology of carcinoma of the breast as seen
in 31 female pts. (aged 49-85; 24 were post-meno-
pausal) and 1 male pt. (aged 46). Of these pts.,
27/32 (84%) had suffered prolonged periods of emo-
tional stress prior to the onset of malignancy.
Case histories of 4 female pts., selected at ran-
dom, are cited as examples. The author concludes
that chronic, severe emotional stress (especially
if accompanied by prolonged physical stress) may
be a factor, and even a decisive one, in the eti-
ology of mammary cancer, while acute stress or
stress occurring over short periods of time is
more likely to predispose to heart attacks or some
types of skin disorder. Suggested as a minimum
period of chronic stressing for induction of mam-
mary cancer is 5-7 yr. The author also concludes
that personality type is not a factor in carcino-
genesis.

64-597 NUCLEAR SIZE IN PREMALIGNANT CONDITIONS
OF THE CERVIX UTERI. (E.) Atkin, N. B.
(Dept. Cancer Res., Mt. Vernon Hosp., Northwood,
Middlesex, England). Nature (London) 202:201, 1964.

Microscopic examination of 87 sections of carcinoma *in situ* of the cervix uteri (mean age of pts. 36.7, range 22-81) revealed large nuclei in 54/77 of the squamous type and in 4/10 of the basocolumnar type; small nuclei were seen in 23/77 and 6/10, resp. Of 24 sections of microcarcinoma of the cervix uteri (mean age of pts. 44.4), large nuclei were seen in 9/19 and 10/19, resp.; small nuclei were seen in 10/19 and 0/5, resp. Of 18 sections of basal cell hyperplasia (mean age of pts. 35.5) 1/18 showed large nuclei and 17/18 showed small nuclei. The findings suggest that either polyploidy with normal tetraploid chromosome complements or aneuploidy with near-tetraploid complements is of frequent but variable occurrence in carcinoma *in situ*, and may occasionally be prominent in even earlier stages of carcinogenesis. Suggested as meriting investigation is the question as to whether nuclear size (or DNA content) may be of prognostic significance in carcinoma *in situ*.

- 64-598 STUDIES ON A TRANSPLANTABLE MASTOCYTOMA IN MICE. II. ELECTRON MICROSCOPIC OBSERVATIONS. (E.) Christensen, H. E. (University Inst. Path. Anat., U. Copenhagen, Denmark), O. H. Iversen and R. Rask-Nielsen. *J. Nat. Cancer Inst.* 30(4):763-781, 1963.

Electron microscopic studies of a highly differentiated, transplantable, mouse mast cell neoplasm (taken from hosts 7-10 mo. after they had been inoc. s.c. with tumor tissue) revealed the following: mast cells showed a highly organized endoplasmic reticulum; mast cell granules located in the outer zone of the cytoplasm in most cells and appearing in all transitional stages of maturity from loose curls to condensed, homogeneous material; a well developed Golgi region; long, slender protrusions projecting from the cell surface; numerous ribosomes, free or attached to membranes; a smooth membrane-like inner surface in the lacunae which lodged the mast cell granules. It was suggested that a direct connection may exist from the interior of the mast cell through the channels of the endoplasmic reticulum to the lacunae, and from the lacunae, during the release of the mast cell granules to the extracellular space.

- 64-599 ABNORMAL CELLULAR RESPONSE TO SKIN ABRASION IN CANCER PATIENTS. (E.) Dizon, Q. S. (Sloan-Kettering Inst. Cancer Res., New York) and C. M. Southam. *Cancer* 16(10):1288-1292, 1963.

A mild abrasion (without bleeding) was produced by lightly sandpapering the skin of 83 pts. with advanced cancer (widely disseminated breast, lung, g.i., uterine or ovarian); 18 pts. with early (non-metastasized uterine, ovarian or breast) cancer; and controls that were healthy, acutely or chronically ill. Differential cell counts were made on the resulting cellular exudates serially collected on glass coverslips at 3-48 hr. later. At 3 and 6 hr. there was a predominance of neutrophils in all subjects. Thereafter, macrophages predominated in the healthy controls and in pts. with early cancer (who may have been surgically cured) or with diseases other than cancer. Advanced cancer pts. showed a preponderance of neutrophils even at 21-48 hr. Chemotherapy or X-ray treatment did not seem to affect the results. It is suggested that cancer pts. have an impaired capacity to mobilize tissue macrophages. This phenomenon was found to be correlated with, but not necessarily causally related to, the impaired capacity of advanced cancer pts. to reject homo-transplants.

- 64-600 STIMULATION OF THE GROWTH OF SPONTANEOUS HEPATOMAS BY LIVER REGENERATION. (Fr., Abstract) Echave Llanos, J. M. (Inst. Gen. Exptl. Path., Dept. Med., U. Mendoza, Argentina) and I. E. Saffe. *C. R. Soc. Biol.* 157(10):1807, 1963.

The incidence of spontaneous hepatomas at 17 mo. of age was studied in 143 male C3H/mza mice: 84/143 untreated, 44/143 hepatectomized (70%) at the age of 9 mo., and 15 hepatectomized twice, the first time at the age of 9 mo. with removal of the median lobe (33% of liver) and the second time at the age of 12 mo. with removal of the left lobe (35%). Hepatectomized mice developed a higher number of tumors than intact mice and their tumors were larger (13.6 mm; controls 6.2 mm). Histologically, the degree of malignancy was higher in the hepatectomized mice, especially in those which had undergone repeated hepatectomy. (See also CRA 1(11):#2026, 1964.)

ERRATA:

Cumulative Author Index, under Hamazaki, Y, correct 1864 to read 1846.

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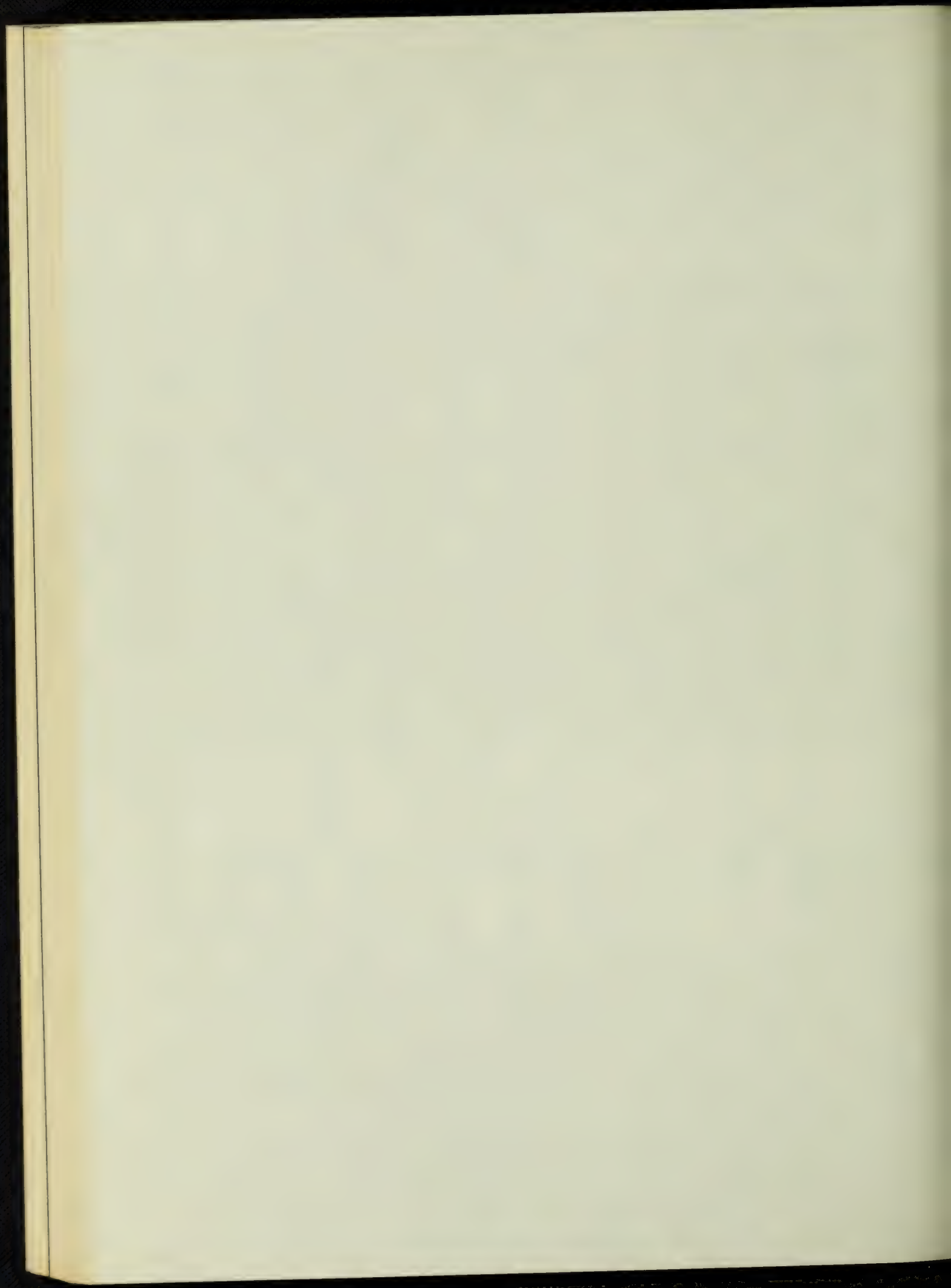


CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS

ABSTRACTS

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum, maximal
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubate(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

601 CARCINOGENIC EFFECTS OF ^{131}I COMPARED WITH X-IRRADIATION--A REVIEW. (E.) Senger, E. L. (Dept. Radiol., U. Cincinnati Coll. Med., Ohio), R. A. Seltzer, T. D. Sterling and J. G. Kereiakes. *Health Phys.* 9(12): 1371-1384, 1963.

After a retrospective and prospective review of the induction of thyroid cancer in adults and children following external X-irradiation, whole and partial body γ -neutron irradiation, the authors discuss the effect of β - γ -irradiation with ^{131}I on thyroid carcinoma in adults and the increased susceptibility to neoplastic changes in the thyroid of children following ^{131}I . It is concluded that neoplastic response of ^{131}I compared to X- or γ -irradiation is primarily a function of differences of dose rates and tissue distribution, but further studies are necessary before the importance of these factors can be fully evaluated. (53 references)

602 THE RELATIONSHIP BETWEEN RADIATION DOSE DELIVERED TO THE THYROIDS OF CHILDREN AND THE SUBSEQUENT DEVELOPMENT OF MALIGNANT TUMOURS. (E.) Dolphin, G. W. (United Kingdom Atomic Energy Auth., Harwell, Didcot, Berkshire, England) and S. A. Beach. *Health Phys.* 9(12):1385-1390, 1963.

A quantitative dose-response relationship found in a literature survey of children given X-irradiation in early infancy is used to determine the dose-response relationship of ^{131}I . Some additional conclusions are drawn: to produce a given incidence of malignant thyroid tumors in children, the radiation dose from ^{131}I would be approximately 10 times higher than that from X-irradiation. Thus, the estimated total incidence/10⁶ rad from ^{131}I is 35, as compared to 3.5 from ^{131}I ; the risk of inducing malignant thyroid tumors in children by ^{131}I is about the same as that for leukemogenesis by acute external irradiation in adults and may be less than that for leukemogenesis by X-irradiation *in utero*; a child's thyroid is not specially sensitive to radiocarcinogenesis compared with the blood-forming organs. (27 references)

603 BIOLOGICAL ASPECTS OF THEORETICAL NEURO-ONCOLOGY. (Rus) Avtsyn, A. P. (Inst. Human Morph., Acad. Med. Sci. USSR, Moscow). *Ark. Pat.* 25(12):3-22, 1963.

In this review article on theoretical neuro-oncology are discussed the occurrence and development of the tumors of the central nervous system, the dependence of brain tumors on the period of individual development, and on the sex of the patient, the classification of brain tumors in relation to various etiologic factors and the role played by disturbances in hormone balance. (93 references)

64-604 MALIGNANT TUMORS AND THEIR HEMOGRAMS AS A REFLECTION OF MODIFYING INFLUENCES OF THE VEGETATIVE NERVOUS SYSTEM. (Ger.) Schlitter, H. E. (Inst. Radiol., Moabit Hosp., Berlin). Pp. 88-94 in *German Congress of Radiology 1963 (Deutscher Röntgenkongress 1963)*. 44th Congr. Germ. Radiol. Vol. 55(b) (spec. edit. of *Strahlentherapie*). Bauer, R. (Ed.). Urban & Schwarzenberg, Berlin. 381 pp., 1964.

An extensive review of the literature on increased activity of the autonomic nervous system in the precancerous, premetastatic, and tumorous stages of malignancies refers to various theories of carcinogenesis and attempts to supplement or clarify these by a discussion of the modifying influences of the autonomic nervous system on tumor-growth and metastasis. (184 references)

64-605 PATHOGENESIS AND CONTROL OF BREAST CANCER. (E.) Furth, J. (Dept. Pathol., Columbia U. Coll. Physicians Surg., New York). *Bull. N.Y. Acad. Med.* 40(6):423-431, 1964.

In a discussion of the control of breast cancer (mainly by endocrine ablation), the author noted that hormones of the pituitary play a determining role in the formation of mammary tumors by the three classes of carcinogens (viruses, certain chemicals and radiation) and in the growth of many of the induced tumors. Small doses of carcinogens which are incapable of producing mammary tumors alone, readily do so when the mammary gland is stimulated by the mammotropic hormones. The main promoters of human mammary tumor are those agents which stimulate the mammary gland and therefore increase the chance of retention of carcinogenic substances and increase the sensitivity of the cells to carcinogenic modification by increasing the number of carcinogen-sensitive mitotic stages. (15 references)

64-606 LUNG-BRONCHIAL CANCER AND THE INFLUENCE OF THE ENVIRONMENT. (Ger.) Maurer, H.-J. (Dept. Roentgenol., Clin. Surg., U. Bonn, Germany). *Strahlentherapie (München)* 123(3): 392-411, 1964.

A brief discussion of the more common carcinogens encountered in everyday life, particularly in industrial situations (polycyclic aromatic hydrocarbons, aromatic amines, alkylating agents, urethan, croton oil, turpentine, creosote oil, plastics such as the polystyrenes (-amylates, -anthylenes, etc), and inorganic compounds of As, Cr, Be, and asbestos), is followed by a detailed review of population studies and statistical documentation of the increase of lung and bronchial malignancies. Special emphasis is placed on smoking and on its relative contribution to the increasing incidence. It is pointed out that the av. yearly 3,4-benzpyrene conc. per 100 m³ (correction for cm³) air is about 4.2 μg

(in Sheffield, England), 17 μg during smog days; that it is 30 $\mu\text{g}/100\text{ g}$ in soot and only 0.02 $\mu\text{g}/100\text{ g}$ of tobacco. Thus, while tobacco is an important factor, it is felt that the increase in atmospheric contamination caused by technical developments and increasing industrialization is a primary factor in the syncarcinogenesis of lung and bronchial cancer. (127 references)

- 64-607 THE EFFECT OF CHRONIC RADIATION EXPOSURE ON THE HEMATOPOIETIC SYSTEM. (Ger.) Faber, M. Pp. 42-48 in German Congress of Radiology 1963 (Deutscher Röntgenkongress 1963). 44th Congr. Germ. Radiol. Vol 55(B) (spec. edit. of Strahlentherapie). Bauer, R. (Ed.). Urban & Schwarzenberg, Berlin. 381 pp., 1964.

In a review of the effects of chronic radiation exposure on the hematopoietic system, report is made that leukemic deaths have been observed in only 4/1000 persons in Denmark who received inj. of Thorotrast; 2/4 had also received radiotherapy and some had been receiving medications (not specified) which are known to be leukemogenic. In only 1 case could Thorotrast be considered the only probable cause. The total number of living persons who have received Thorotrast is estimated at 50,000-100,000. A survey of data reported in the USA and England indicates only 2 cases of chronic leukemia (1 lymphatic, 1 myeloid) among 985 pts. bearing radium implants; and the author points out that only the lymphatic leukemia could possibly be attributed to radiation. (Reported as previously occurring among these same pt. groups were 2 cases of acute and 1 of chronic myeloid leukemia + 1 case of splenic leukemia.) On the basis of these and other reports in the literature, the total number of living persons bearing such implants is estimated as at least 3,000-4,000. The author concludes that alleged leukemogenic effects of Thorotrast, radium implantation and Sr^{90} fallout are at the least highly questionable. (25 references)

- 64-608 TRENDS IN CANCER RESEARCH. A HISTORICAL ETIOLOGIC INVESTIGATION. PART II. (Ger.) Lehmann, F. M. (105 Camden Rd., London, N.W.1). Med. Klin. 59(17):707-711, 1964.

A historic review of ideas and theories concerning carcinogenesis and therapy, with some unusually critical and harsh comments concerning radiotherapy, chemotherapy and their theoretical bases. However, hope is expressed for the future of cancer research provided that currently held ideas concerning cellular and tissue proliferation, would give way to an "ontogenetic approach", and would shift the blame from the proliferating cell to its relationship with its surrounding medium, i.e., with the organism as a whole. (37 references)

- 64-609 EXPERIMENTAL IMMUNIZATION AGAINST CARCINOGEN-INDUCED AND VIRUS-INDUCED MOUSE TUMORS IN ISOLOGOUS OR AUTOLOGOUS SYSTEMS. (E.) Sjörgen, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). Pp. 459-474 in Conceptual Advances in Immunology and Oncology. A collection of papers presented at the 16th Annual Symposium on Fundamental Cancer Research, 1962, U. Texas M.D. Anderson Hosp. and Tumor Inst., Houston. Hoeber Med. Div. Harper & Row, Publ., Inc., New York. 557 pp., 1963.

A review of experimental studies by the author and others demonstrating the existence of tumor-specific antigens in various experimental tumors. Methylcholanthrene-induced sarcomas (MCS) contain tumor antigens that are not only specific to the tumor type but, in most cases, seem specific to each individual tumor. Cross reaction experiments with mice using 2 different MCS strains (MC57G and MC57F) inoc. into isologous recipients, subsequent to total body irradiation, showed no cross-resistance between the two sarcomas. Neutralization experiments using lymph node cells gave the same negative results. Polyoma virus-induced tumors (PT; s.c. and osteogenic sarcomas), on the other hand, seem to possess a common polyoma tumor-specific cellular antigen. Groups of mice pretreated with these PT homografts (or homografts of MCS or spontaneous mammary tumors), and then subjected to PT isografts, failed to demonstrate cross resistance between PT and other tumor types. Preliminary neutralization experiments indicated that lymph node cells of virus-immunized animals were capable of neutralizing PT cells, after the 2 were mixed and inoc. into isologous untreated animals. The weaker antigenic response of lymphomas (LG) induced by Gross virus appears to be tumor specific with some cross resistance between individual tumors. Transplantation of PT and LG into isologous recipients pretreated with polyoma virus, PT homografts or LG homografts showed no evidence of cross reaction of LG with lymphomas of other origins. The possibility that tumors of known viral origin may contain infectious virus or at least part of the virus genome is discussed. (See also CRA 1(5):#898, 1963; ibid., 1(11):#1970, 1964.) (22 references)

- 64-610 IMMUNITY TO VIRUS-INDUCED TUMORS. (E.) Sjörgen, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). Canad. Cancer Conf. 5:377-386, 1963.

See CRA 1(5):#898, 1963; and ibid., 2(4):#609, 1964. (25 references)

- 64-611 GROWTH CONTROL OF NERVE CELLS BY A PROTEIN FACTOR AND ITS ANTISERUM. (E.) Levi-Montalcini, R. (Dept. Zool., Washington U., St. Louis, Mo.). Science 143:105-110, 1964.

A review of the experimental work leading to the

discovery of a growth promoting protein (NGF) in mouse sarcomas (and subsequently in snake venom and mouse salivary glands) is presented in view of the developmental and neurogenetic processes that this might clarify. Fragments of Sarcoma 180 or Sarcoma 37, if grafted onto the chorioallantoic membrane of 4-6-day chick embryos, selectively enhanced the nerve fiber outgrowth from the sensory and sympathetic ganglia of the host. Furthermore, when sympathetic ganglia of 7-9-day embryos are cultured with fragments of these same sarcomas, within 5 hr. these ganglia are surrounded by a dense halo of nerve fibers which increased in density and length during the following 24 hr. Controls produced only few sparse nerve fibers. An antiserum of NGF has been developed which blocks the differentiation and development of sympathetic ganglia. (22 references)

612 CANCER: AN ENVIRONMENTAL DISEASE. (E.) Wade, L. (Sloan-Kettering Inst. Cancer Res., N.Y.). S. Afr. Cancer Bull. 8(1): 1-23, 1964.

riefly discussed, is a review article which was previously abstracted as CRA 1(8):#1420, 1963. (0 references)

613 NINETEENTH CENTURY FOUNDATIONS OF CANCER RESEARCH. ORIGINS OF EXPERIMENTAL RESEARCH. (E.) Triolo, V. A. (McArdle Chem. Lab., U. Wisconsin Sch. Med., Madison). Cancer Res. 24(1):4-27, 1964.

a very extensive review of the origins of experimental cancer research, the classic induction theory of cancer (bacterial, protozoan, plant, mycetozoan and virus theories), studies of tumor transmission and studies on tumor growth are discussed. This paper was designed principally as a guide to 19th century cancer research which was surveyed along the broadest lines. Hirst's work of 1882-83 ranks among the first experimental attempts to produce cancer through irritative stimulus (oil of sweet almond converted into an irritant by the addition of croton oil). Fischer's investigations, beginning in 1915, on the carcinogenicity of Scharlach R and other dyestuffs formed the basis from which the irritation idea was gradually generated into the modern field of experimental carcinogenesis. (4 references)

614 TUMOUR-VIRUSES AND VIRUS-TUMOURS. (E.) Andrewes, C. Brit. Med. J. 1:653-658, 1964.

author documents the existence of tumor-viruses with a review of the literature on the Rous mouse mammary virus, Gross leukemia virus, Shope papilloma virus, Rous sarcoma virus, and SV40. The present state of the

relationship between viruses and human cancer is also discussed. (16 references)

64-615 THE CHALLENGE OF CANCER. (E.) Silliphant, W. M. (Dept. Path., U. California Sch. Med., San Francisco). J. Occup. Med. 6(3):115-122, 1964.

Brief review dealing with the etiology of cancer (known carcinogens; environmental and occupational factors); the changing mortality rates in the U. S. for lung, uterine cervix, and stomach cancer; and modern cancer therapy and prevention. At the present moment the author concludes, hope lies in the avoidance of certain known agents, public education to seek early diagnosis and treatment, and continued cancer research. (25 references)

64-616 ASPECTS OF METAPLASIA IN GENITO-URINARY PATHOLOGY. (E.) Towers, R. P. (St. Vincent's Hosp., Dublin). J. Irish Med. Assn. 53(318):179-183, 1963.

In a review of metaplasias of the female genito-urinary tract, the author suggests that mucinous ovarian cystadenomas appear to arise from metaplastic germinal epithelium just as serous ones do. Cited as an example is a 43-year-old pt. whose left ovary contained a typical, small mucinous cystadenoma and whose right ovary appeared normal externally, although serial section showed a very early mucinous cystadenoma demonstrating all stages of transition from frankly germinal to frankly mucinous epithelium. Also cited are several cases of transformation of pyelitis glandularis into adenocarcinoma of the bladder, with foci of pyelitis cystica in continuity with the mucinous epithelium in such fashion as to suggest that these foci were all proliferative and metaplastic in response to chronic inflammation. (29 references)

64-617 AIR POLLUTION AND PUBLIC HEALTH. (E.) Katz, M. (Dept. Natl. Health Welfare, Ottawa, Canada). Occup. Health Rev. 15(4):8-13, 1963.

In a review and discussion of the effects of chronic and acute air pollution on public health, polluted community atmosphere was classified into 2 types: reducing and oxidizing. Reduced atmospheres are characterized by high conc. of smoke, other suspended particles and sulfur dioxide, such as in London, England. Oxidizing atmospheres have high conc. of hydrocarbons, nitrogen oxides, and ozone or "oxidants"; the latter two are formed photochemically by the action of sunlight on nitrogen oxide and hydrocarbons, with motor exhaust gases a major contributor, such as in Los Angeles. Specific air pollutants such as ozone and sulfur dioxide were shown to be toxicants experimentally. From urban air pollution, 16 mg of 3,4-benzpyrene, a quantity 40,000 times greater than that capable

of producing cancer in mice experimentally, has been estimated to be retained or inhaled in lungs during a lifetime. Conc. of 3,4-benzpyrene and other hydrocarbons in the community atmosphere in North America are much lower than levels reported for cities and town in England and in some European urban centers. (16 references)

- 64-618 THE ORGANIC FRACTION OF PARTICULATE POLLUTION INCLUDING POLYCYCLIC HYDROCARBONS. (E.) Katz, M. (Dept. Natl. Health Welfare, Ottawa, Canada) and J. L. Monkman. *Occup. Health Rev.* 16(1):3-16, 1964.

Figures on the widely differing organic fractions of atmospheric particulates upon benzene extraction are reviewed. Particular attention is given to the polycyclic hydrocarbons, methods for their analysis, their content in organic atmosphere pollutants and their carcinogenic activity. The content of organic material in urban atmospheres was found to be higher in winter and lower in summer. Data obtained from cities in the United States, Europe and Canada are discussed. It was shown that the production of polycyclic aromatic hydrocarbons in efficiently operated diesel vehicles was negligible in comparison with the amount of these hydrocarbons formed by general combustion in urban activities. (See also CRA 2(4)#617, 1964.) (38 references)

- 64-619 CIGARETTE SMOKING AS THE MAJOR CAUSE OF LUNG CANCER. PART I. (E.) Oettlé, A. G. (S. African Inst. Med. Res., Johannesburg). *S. Afr. Med. J.* 37(37):935-941, 1963.

In the first of three reports, a review of numerous statistical studies establishes a relationship between cigarette smoking and cancer of the lung. A causal hypothesis for cigarette smoking and cancer is not confirmed, but is supported by study of pathological changes in the bronchial mucosa of smokers and nonsmokers as well as by the results of animal experiments. From his own region, the author notes that among white South Africans deaths due to primary lung cancer have increased over a 10-year period (1949-1958); male deaths have more than doubled. Among gold miners, during the period of January 1957-October 1962, lung cancer comprised 35.9% of all cancers reported. Histological studies of 2 groups of miners indicate the increase is in Kreyberg Type-1 tumors. (No references)

- 64-620 CIGARETTE SMOKING AS THE MAJOR CAUSE OF LUNG CANCER. PART II. (E.) Oettlé, A. G. (S. African Inst. Med. Res., Johannesburg). *S. Afr. Med. J.* 37(38):958-963, 1963.

The second of three reports presents further statistical data on the relationship between cigarette smoking and lung cancer; it also furnishes material on other factors, besides the

cigarette smoke itself, with which lung cancer might be correlated. Statistical analyses have shown a greater mortality in smokers in large cities than in those from rural areas; however, the relation between duration of smoking and increase in risk is not clear. (No references)

- 64-621 CIGARETTE SMOKING AS THE MAJOR CAUSE OF LUNG CANCER. PART III. (E.) Oettlé, A. G. (S. African Inst. Med. Res., Johannesburg). *S. Afr. Med. J.* 37(39):983-987, 1963.

The third of three reports on cigarette smoking and lung cancer recommends a frank admission of the dangers of smoking, an intensive health education campaign, an increase in taxation on various cigarettes in proportion to the amount of tar present and a limitation on advertising. It is felt that there is no further need for research into the association between lung cancer and smoking; rather, what is needed, is research into the mechanism whereby cigarette smoking causes lung cancer. (113 references)

- 64-622 POLYCYCLIC HYDROCARBONS. (E.) Boyland, E. (Chester Beatty Res. Inst., London). *Brit. Med. Bull.* 20(2):121-126, 1964.

A review and discussion is presented on polycyclic hydrocarbons, direct and indirect carcinogens, the metabolism of polycyclic hydrocarbons (phenanthrene and 1,2-benzanthracene and their metabolites), metabolic reactions as an inactivation process, the possible active metabolites of aromatic hydrocarbons, the complexes of aromatic carcinogens and purines, the complexes of aromatic carcinogens with nucleic acid, and carcinogenesis by deletion of repressors. The polycyclic hydrocarbons are generally, but not always, local in their action (local application produced epitheliomas of the skin, implantation in the bladder induced bladder cancer, inj. induced sarcoma). None of the many known metabolites of carcinogenic hydrocarbons were found to be active and it is not known with certainty if these metabolites of hydrocarbons are precarcinogens or proximate carcinogens. The author indicates that it is possible that carcinogenesis by chemicals is due to destruction of suppressors which control function and synthesis in normal cells, so that these become malignant. (52 references)

- 64-623 NATURAL, METALLIC AND OTHER SUBSTANCES, AS CARCINOGENS. (E.) Roe, F. J. C. (Chester Beatty Res. Inst., London) and M. C. Lancaster. *Brit. Med. Bull.* 20(2):127-133, 1964.

An extensive review of the carcinogenic activity of fungal toxins (including aflatoxin), plant toxins, metals (excluding radioactive metals), pharmaceuticals and agricultural chemicals. Details of tissue, species, dose and route of admin. are also considered. (186 references)

624 COCARCINOGENESIS. (E.) Salaman, M. H. (Cancer Res. Dept., London Hosp. Coll. d.) and F. J. C. Roe. Brit. Med. Bull. 20(2): 9-144, 1964.

After defining the term "cocarcinogenesis" and discussing possible modes of action, the authors view various examples of physical, chemical and viral cocarcinogenesis. Isopropyl N-phenyl carbamate and isopropyl N-(3-chlorophenyl)carbamate are recently described tumor initiators for mouse skin; citrus oils (see CRA 1(2):#231, 1963), croton oil (see CRA 2(4):#686; and *ibid.*, 1967, 1964) and anthralin are promoters. Other promoters noted are: urethan on the s.c. tissue of mice; 20-methylcholanthrene and 4-nitro-2-methylcholanthrene on rat liver; 4-ethylsulfonylphthalene-1-sulfonamide and urethan on mouse bladder; citrus oils on the g.i. tract of mice; urethan on mouse RES. Both lung hyperoxia and hypoxia enhance urethan carcinogenesis in mouse lung. It has been suggested the carcinogenesis by cigarette smoke condensate might result from the combined action of initiators and promoters; the phenolic fraction has pronounced promoting activity on mouse skin. Enhanced tumor production by combinations of various carcinogens with oncogenic viruses (Shope papilloma, fibroma, rat sarcoma, polyoma and Graffi leukemogenic viruses) and non-tumorigenic viruses (vaccinia, polio, poliovirus 2 and myxoviruses) is also described. Such a heterogeneous listing suggests that the enhancing effect may arise from basically different processes. (112 references)

625 LYMPH NODE TUBERCULOSIS, PULMONARY TUBERCULOSIS AND PULMONARY CANCER. (E.) Schwartz, P. (Dept. Pathol., State Hosp., Scranton, Pa.). Acta Tuberc. Scand. 44(1):1-38, 1964.

After discussing in great detail the importance of bronchial lesions and lymphonodo-bronchogenic dissemination in pulmonary tuberculosis, the author proceeds to evaluate the frequent relationship between tuberculous pulmonary changes and primary pulmonary neoplasms and reviews cases reported in the literature in which pulmonary malignancies have developed at the level of tuberculous foci. The author feels the importance of cigarette smoking is overemphasized and stresses the importance of tuberculosis and socioeconomic influences in the etiology of certain pulmonary cancers. (79 references)

626 II. THE USE OF RADIOLOGY IN THE EARLY DETECTION OF LUNG CANCER AS AN INDUSTRIAL DISEASE. (E.) Bidstrup, P. L. (Chest Dept., St. Thomas' Hosp., London, S.E.1). Brit. Radiol. 37(437):337-344, 1964.

In connection with a study of the early detection of lung cancer, a brief review is presented of the industries which represent occupational

hazards: work involving exposure to radiations; refining of nickel by decomposition of nickel carbonyl; the manufacture of bichromates from the ore chromite; exposure to asbestos dust; manufacture of coal gas by an obsolete process; and the mining of hematite. The latent period in those affected is long, commonly 20 yr. or more. Of the cases of lung cancer diagnosed from 1955-62 among employees and pensioners of Industry II (hazard recognized after 1954), 50% were diagnosed at annual X-ray examinations; in 40% of the cases death occurred less than 6 mo. after X-ray diagnosis. (6 references)

64-627 IMMUNOLOGY OF EXPERIMENTAL TUMORS. (E.) Old, L. J. (Sloan-Kettering Inst. Cancer Res., New York) and E. A. Boyse. Ann. Rev. Med. 15:167-186, 1964.

The authors review various methods for demonstrating specific antigens in tumors: resistance to tumor challenge, transfer of immunity with immunologically active cells, activity of serum from immunized animals (for cytotoxic technic, see CRA 1(7):#1353, 1963) and immunization of foreign species. A discussion of tumor-specific antigens found in chemically-induced sarcomas (see also CRA 1(7):#1353, 1963) and hepatomas, cellophane film-induced sarcomas, polyoma tumors, mammary tumors, thyroid tumors and in tumors of noninbred species, as well as X-antigen and TL antigen (see also CRA 2(2):#204; and *ibid.*, 2(3):#578, 1964) and antigens associated with Gross, Friend and Moloney viruses, follows. Immunological relationships among murine leukemias are also reviewed. (132 references)

64-628 SOVIET STUDIES IN REGIONAL (GEOGRAPHIC) PATHOLOGY. (E.) Brandt, M. (Dept. Med., Osteuropa Inst., Free U., Berlin). I.C.R.S. Med. Rep. (5):1-62, 1964.

In this monograph on pathology in various regions of the Soviet Union, the author briefly reviews statistics on the incidence of skin cancer, cancer of the mouth, esophageal, mammary, cervical and thyroid carcinomas, based on reports of the AMS Oncological Institute and Health Ministry expeditions and the Leningrad Conference of 1958. (2 pertinent references)

64-629 THE CARCINOGEN 3,4-BENZOPYRENE IN THE LIVING ENVIRONMENT AND HUMAN ORGANISM. (E.) Šula, J. P. (Dept. Med. Chem., Charles U., Prague, Czechoslovakia). Neoplasma (Bratisl.) 10(6):571-579, 1963.

A review and discussion of: the possible penetration of 3,4-benzopyrene (BP) into the human organism through the skin, digestive and respiratory tracts; the work of the author and other investigators which led to the isolation and identification of BP in wood tar from smoke

chambers and in smoked meat and fish; physico-chemical detection of BP in biological material and in the bronchial lymph glands of a brother and sister fed food for about 2 yr. which had been smoked by burning tarred railway ties (sleepers). The importance is stressed of the detection of BP in the environment and in the human organism as an aid in programs for the rational prevention of cancer in the digestive and respiratory systems. (73 references)

64-630 CARCINOGENESIS BY NITROSO COMPOUNDS.
(E.) Magee, P. N. (Med. Res. Coun. Lab., Carshalton, Surrey, England) and R. Schoental. Brit. Med. Bull. 20(2):102-106, 1964.

The chemical characteristics and carcinogenic activity of various nitroso compounds are reviewed as an attempt to define their possible mechanism of action. Both lesions or tumors are described involving the liver, kidney, lung, esophagus and stomach. The impairment of incorporation of amino acids into liver proteins suggests that dimethylnitrosamine damages microsomal structures. This alteration may be related to its ability to methylate liver proteins and nucleic acids. Although the nitroso compound itself may be the actual carcinogen, evidence seems to indicate that a decomposition product (possibly an alkylating agent) is the proximate carcinogen. (See also CRA 1(12):#2098, 1964.) (101 references)

64-631 THOUGHTS ON THE MANAGEMENT OF CARCINOMA.
(Ger.) Meythaler, F. (2nd Med. Clin., City Hosp. Nurnberg, Germany). Urologe 3(2): 57-72, 1964.

In a wide-ranging general discussion of the causes and treatment of cancer, there are sections on: geographic patterns of incidence of different types of cancer; environmental (including industrial) carcinogens and cocarcinogens; endocrinological factors; nucleic acid relations, defective cell respiration and psychic factors in carcinogenesis; spontaneous remissions; and current theories on the biochemistry of malignant tumors. The author emphasizes the probably ubiquitous and repeated occurrence of the carcinogenic dedifferentiation of cells (in small numbers), their variable latency, and their control through the body's normal immunologic defenses. (No references)

64-632 HAZARDS AND DAMAGES FROM ROENTGEN RAY EXPOSURE IN CHILDHOOD. (It.)
Limonta, A. (Child. Hosp. Milan, Italy). Lattante 35(3):132-165, 1964.

After a general discussion of somatic and genetic damage from X-irradiation, the author reviews cutaneous, osteo-cartilaginous and gonadal radiosensitivity in children. In the discussion of the hazards of Roentgen therapy and diagnosis in children are included: incidence of thyroid cancer, leukemia and osteochondromas following thymus irradiation; disturbances in bone growth; vertebral column alterations following irradiation of Wilms's tumors, hypernephromas, etc.; incidence of cutaneous and osteocartilaginous changes, mammary hypoplasia or aplasia, cataract and thyroid cancer following irradiation of hemangiomas of the skin and mucosa. Particular reference is made to the relationship between thymus irradiation and thyroid tumors. Hazards were found to depend on the dose and technic of irradiation and caution is recommended. (No references)

See also abstract nos.: 671,694,743,759

PHYSICAL CARCINOGENESIS

633 THE TISSUE REACTION INDUCED IN RATS AND GUINEA-PIGS BY POLYMETHYLMETHACRYLATE (ACRYLIC) AND STAINLESS STEEL (18/8/Mo). (.) Stinson, N. E. (Dept. Biomechanics, U. London, England). *Brit. J. Exp. Path.* 45(1): 1-29, 1964.

Stainless steel and polymethylmethacrylate discs (approx. 18, 12 and 4 mm in diameter) were implanted into the gluteal muscles of 133 guinea pigs (Hartley, 4-6 mo. old) and 212 rats (Chesteratty strain, 3 mo. old). The fibrous tissue capsules which developed around all the implants became thinned in the case of those in the guinea pigs after prolonged implantation and no carcinogenic activity was detected. In rats 51 tumors developed in the fibrous tissue surrounding the large and medium acrylic discs of 46 rats; 7 tumors occurred in relation to the large and medium steel discs in 6 rats. The latent period of tumor formation in the acrylic experiment was 150-807 days and in the stainless steel experiment 332-589 days. Malignant tumor changes were not found in the small disc capsules. Malignant tumors had anaplastic and pleomorphic cells, bizarre mitotic figures and infiltrative growth in the surrounding muscle. In 13 animals, metastatic deposits were found in the lungs and/or in the mesenteric glands; muscle fibers were present in the metastases from the tumors staining muscle. Histologically, all the tumors consisted of spindle cell connective tissue (some containing bone or muscle). The evidence suggests that the thickness and relative vascularity of the fibrous tissue in the rats may be of importance in the production of foreign body tumors in this species.

634 MORPHOLOGY OF MAMMARY GLAND TUMORS INDUCED WITH RADIOACTIVE NIOBIUM. (.) Ponomar'kov, V. I. (Acad. Med. Sci. USSR, Moscow). *Ark. Pat.* 25(12):44-51, 1963.

Radioactive niobium (Nb^{95} ; 6 μ C/g i.p.) was administered to 210 white female rats (80-120 g). First appearance of mammary tumors was noted on day 164 in controls on day 487 after treatment. Initially the tumors were single nodes, and malignant in character; later tumors, appearing on days 300-350, were multiple and benign. Tumors were evenly distributed in all pairs of glands, no symmetry was observed in multiple tumors. Histologic studies were reported in detail: 10% were either fibroadenomas or adenofibromas; 10% were adenocarcinomas with pronounced cellular polymorphism; 2.2% were sarcomas of immature structure; 17.4% were fibrocystic mastopathies. During 700 days of observation, tumors developed in 8% of animals that survived until the time of appearance of the first tumor.

635 INDUCTION OF NEOPLASMS IN THYROID GLANDS OF RATS BY SUBTOTAL THYROIDECTOMY AND

BY THE INJECTION OF ONE MICROCURIE OF I^{131} . (E.) Goldberg, R. C. (Dept. Physiol., U. California, Berkeley), S. Lindsay, C. W. Nichols, Jr. and I. L. Chaikoff. *Cancer Res.* 24(1):35-43, 1964.

Female Long-Evans rats (5-6-week-old) were treated as follows: Group 1, untreated controls; Group 2, subtotal thyroidectomy; Group 3, subtotal thyroidectomy + i.p. inj. of 1 μ C of I^{131} in 0.1 ml of a 0.9% NaCl soln. 1 wk. after thyroidectomy; Group 4, subtotal thyroidectomy + inj. of I^{131} + desiccated thyroid diet (conc. of 250 mg/kg started 1 wk. after I^{131} inj.); Group 5, subtotal thyroidectomy + desiccated thyroid; Group 6, inj. of I^{131} ; Group 7, desiccated thyroid; Group 8, inj. of I^{131} + desiccated thyroid. At the end of 2 yr., results were as follows: adenomas in 8/68 (12%) of Group 2, 13/49 (26%) of Group 3, 3/61 (5%) of Group 4 and 2/41 (5%) of Group 5; alveolar or lobular carcinomas in 13/48 (27%) of Group 1, 3/68 (4%) of Group 2, 17/48 (35%) of Group 6, 21/57 (36%) of Group 7 and 11/46 (24%) of Group 8; papillary carcinomas in 2/68 (3%) of Group 2, 1/61 (1%) of Group 4 and 1/46 (2%) of Group 8; follicular carcinomas in 1/48 (2%) of Group 6.

64-636 LATE SOMATIC EFFECTS OF X-RADIATION IN MICE TREATED WITH AET AND ISOLOGOUS BONE MARROW. (E.) Cosgrove, G. E. (Oak Ridge Natl. Lab., Tenn.), A. C. Upton, C. C. Congdon, D. G. Doherty, K. W. Christenberry and D. G. Gosslee. *Radiat. Res.* 21(4):550-574, 1964.

Young adult female (101 x C3H)F₁ mice were subjected to whole body X-irradiation (350-1800 r; dose rate 80-90 r/minute) with or without the admin. of S,2-aminoethylisothiuronium·Br·HBr (AET) before irradiation and/or isologous bone marrow (IBM) after irradiation. Sixty-day survivors were observed until death and then examined pathologically. Overall tumor incidence was: Non-irradiated, 66% (ovary 30%, lung 21%, uterus 11%); Irradiated (350-800 rads), 75-84% (ovary 54-73%, lung 9-16%, breast 2-11%); Irradiated (500-1,400 rads) + AET, 52-86% (ovary 34-67%, lung 8-14%, uterus 4-12%); Irradiated (500-1,200 rads) + IBM, 51-90% (ovary 31-65%, breast 4-9%, liver 2-8%); Irradiated (500-1,800 rads) + AET + IBM mice, 20-93% (ovary 10-73%, breast 0-17%, orbital 0-7%, reticular 2-9%). Histologic studies of some of the various tumors showed the following types: 108 ovary (54 granulosa cell, 33 mixed, 12 adenofibromas, 9 luteomas); 20 uterus (13 sarcomas, 3 fibroid, 3 fibroadenomatous polyps, 1 carcinoma of the endometrium); 29 breast (4 sarcomas, 1 carcinosarcoma); 20 tubular adenomas of the kidney; unspecified numbers of unencapsulated hepatomas; 20 mixed carcinomatous and sarcomatous salivary gland tumors; 3 gastric tumors (2/3 squamous cell carcinoma, 1/3 sarcoma with liver metastasis); 1/4 adenocarcinoma of the small intestine; 8 adrenal (4/8 pheochromocytomas, 4/8 cortical adenomas); 12/24 osteosarcomas; skin and s.c. tissue tumors

(squamous cell carcinomas and fibrosarcomas, resp.); 8 orbital (8/8 papillary adenocarcinomas). AET and IBM protected against some but not all delayed somatic effects of whole-body X-irradiation, although in no case did the protection appear to afford a factor of dose reduction approximating that obtained against the acutely lethal effects of the radiation.

- 64-637 LIFE SPAN, TUMOR INCIDENCE, AND INTER-CAPILLARY GLOMERULOSCLEROSIS IN THE CHINESE HAMSTER (*CRICETULUS GRISEUS*) AFTER WHOLE-BODY AND PARTIAL-BODY EXPOSURE TO X-RAYS. (E.) Kohn, H. I. (Harvard Sch. Med., Boston, Mass.) and P. H. Guttman. *Radiat. Res.* 21(4):622-643, 1964.

Chinese hamsters were subjected to whole body (WB; 42 rads/min.), anterior (AB) or posterior (PB) partial body X-irradiation (35 rads/min.); mean age at exposure was 133 days. A total of 49 tumors (in 37 animals) was found in 309 autopsied animals, giving an overall incidence rate of 0.16. The most frequent tumor sites (and histologic types), based on 49 total tumors, after WB, AB and PB X-irradiation were as follows: ovary 18 (8 theca cell, 4 granulosa cell, 2 luteoma, 2 mixed); adrenal cortex 2, controls 4; liver 3, controls 5 (7 hepatoma, 1 cystadenoma); kidney 3 (2 adenocarcinoma, 1 clear cell carcinoma); testis 3 (3 Leydig cell); lymphoma group 3 (2 lymphoblastic, 1 lymphocytic); squamous cell carcinoma of the skin 1. In controls, a total of 16 tumors were noted in 112 autopsies. Three cases of leukemia in irradiated animals occurred after WB exposure, as compared to 1 case in controls. In the male, gross tumor incidence rate was not increased significantly by irradiation, but in the female, the most striking effect was the significantly increased incidence of ovarian tumors when the ovary was irradiated by either WB or PB exposure. Since the Chinese hamster has a low spontaneous rate of tumor incidence and is susceptible to tumor induction by irradiation, it should prove to be a valuable animal for radiobiological studies. (See also CRA 1(2):#187, 1963.)

- 64-638 BIOLOGICAL EFFECT OF STRESS FOLLOWING IONIZING RADIATION. (E.) Gambino, J. J. (Dept. Radiol. Path., U. California Sch. Med., Los Angeles), L. R. Bennett, M. S. Billings and B. G. Lamson. *Aerospace Med.* 35(3):220-224, 1964.

The effects of repeated stress-producing stimuli following sublethal irradiation was studied in 4-month-old female Long-Evans rats: 61/195 (Group 1) received whole body X-irradiation (500 r); 70/195 (Group 2) received β -irradiation (500 r) of the surgically exposed adrenal glands; 64/195 (Group 3) served as nonirradiated controls. Surviving animals, 4 mo. after irradiation, were either exposed to intermittent cold (3 hr./day

at $0^\circ \pm 1^\circ\text{C}$) or kept at a temperature of $25^\circ\text{C} \pm 2^\circ\text{C}$. There was no significant difference in the number of palpable tumors in cold- and normal-temperature-treated rats of Group 1; however, there was a lower percentage of tumor-bearing rats among cold-treated animals (56 as compared to 71) which after 17-18 mo. was significant at the 5% level. In Group 2, the percentage of tumor-bearing rats and total tumors was 44 and 66, resp., for animals exposed to normal temperatures and 37 and 48, resp., for those exposed to cold. As compared to controls, animals of Group 2 showed slightly accelerated mammary gland enlargement and appearance of palpable tumors.

- 64-639 ELECTRON MICROSCOPY OF THE THYROID TUMORS INDUCED BY IODINE DEFICIENCY IN RATS. (E.) Lupulescu, A. (Dept. Endocr., U. Bucharest, Rumania) and A. Petrovici. *Folia Endocr. (Pisa)* 16(1):105-122, 1963.

Electron microscope studies in ^{131}I -treated male rats bearing thyroid tumors induced by prolonged low iodine diet revealed ultrastructural changes in the ergastoplasm, mitochondria and nuclei of thyroid cells, the intensity of which paralleled the duration of iodine deficiency. A low ^{131}I -uptake was noted in the above cells. These findings are helpful in clarifying the histogenesis of thyroid tumors.

- 64-640 CARCINOGENIC EFFECTS OF THOROTRAST IN EXPERIMENTALLY PRODUCED CHRONIC RADIATION SICKNESS. (Rus.) Chalisov, I. A. and A. N. Kishkovskii. *Med. Radiol.* 8(10):65-71, 1963.

A study was made on 245 rabbits (no details) of which 210 received daily whole body multiple X-irradiation. Thorotrast (T; multiple admin. each 2-3 ml into the soft tissue of the foot), employed as a contrast medium for intravital lymphography, was given to 155 irradiated and 30 control rabbits. In the rabbits with irradiation disease changes occurred at the site of the inj. of T. In 16 necrosis was evident, while 14 showed dense formations of which 8 were sarcomas with metastases to the lungs, liver, spleen, kidneys and other organs. Six rabbits showed T-granuloma. There was a relation between time of tumor appearance and the schedule and intensity of the radiation admin. With a small radiation dose for longer periods of time tumors appeared about 12-14 mo. after the first T inj.; with more intensive, but shorter irradiation tumors appeared 21-22 mo. after the first T inj. No tumors were found in controls which received even larger doses of T; some showed atrophy and inflammation of the skin and occasionally there was some slight necrosis.

- 64-641 ULTRAVIOLET ABSORPTION IN EPIDERMAL CANCER CELLS. (E.) Kametsky, L. A. (I.B.M. Watson Res. Ctr., Yorktown Heights, N. Y.), H. Derman and M. R. Melamed. *Science* 142:1580-1583, 1963.

idence of the "excessive functional activity" of some cancer cells first found by Caspersson relative to absorption of RNA and DNA at 260 mμ and certain proteins at 280 mμ) has been observed. Fixed, stained smears of cervical epidermoid carcinomas in 4 pts. Preliminary results suggest that there may be a characteristic difference between the absorption profiles of some epidermoid cancer cells and other cells found in cytological smears. The authors conclude that with an appropriate electronic scanning system, such cells could be detectable by measurements of their absorptions at 2 different wavelengths. However, the effect on cellular absorption profiles of abnormalities other than cancer, and whether every epidermoid carcinoma will contain cells showing characteristic absorption profile differences, must yet be determined.

642 THE PATHOLOGY OF MESOTHELIOMATA AND AN ANALYSIS OF THEIR ASSOCIATION WITH ASBESTOS EXPOSURE. (E.) Hourihane, D. O'B. (pt. Path., London Hosp. Sch. Med.). Thorax 33:268-278, 1964.

a review of all the cases from 1917-1962

recorded as primary diffuse tumors of the pleura or peritoneum (mesotheliomas) in the necropsy files of the Bernhard Baron Institute of Pathology at the London Hospital, 38 tumors were filed as primary pleural mesotheliomas, and 17 were selected for pathologic report. In Group A (4 males, 3 females, age 37-77 yr.), with structure typical of mesotheliomas, 6/7 had asbestos bodies in the lungs, all had tumor plaques in the peritoneum, 5 showed metastases within the lymph nodes, 2 in the axillary nodes. In Group B (9 males, 1 female, age 23-74 yr.), 1/10 had asbestos bodies in the lungs, 6 had peritoneal tumors, 2 had lymph node metastases, 2 had interlobar and intrabronchial tumor extension, and 2 showed metastases in the axillary nodes. Group B tumors showed histologic features which were not typical of mesotheliomas. Of 55 tumors filed as primary peritoneal mesotheliomas, 13/55 (Group C) were classified as "certain" peritoneal mesotheliomas, and 4/55 (Group D) as "probable" peritoneal mesotheliomas. In Group C, 7/13 had asbestos bodies in the lungs, 1 had lymph node and 1 axillary node metastases. In Group D, 1/4 had asbestos bodies in the lungs, 1 had lymph node metastases. Of the 37 peritoneal tumors rejected as mesotheliomas, none had observable asbestos bodies in the lungs.

See also abstract nos.: 601,602,605,607,608, 626,632,672,706,714

CHEMICAL CARCINOGENESIS

64-643 LOCALIZATION OF LIVER SPECIFIC ANTIBODY IN NORMAL AND 3'-DAB-TREATED RATS.

(E.) Green, H. N. (Dept. Exptl. Path. Cancer Res., U. Leeds, England) and T. Ghose. Nature (London) 201:308-309, 1964.

Adult Sheffield rats (200-250 g) of both sexes were treated with i.p. inj. of 3'-methyl-4-dimethylaminoazobenzene (3'-DAB; 20 mg/100 g in arachis oil) and with appropriately absorbed antisera (0.5 ml/200 g inj. into the internal jugular vein) against normal rat liver and against 3'-DAB-treated rat liver prepared from rabbits; the rats were sacrificed after 1 hr. The anti-normal rat liver serum stained both hepatic cells and Kupffer cells of normal rat liver, with localization in the former on the cell membrane and around the nucleus. The anti-normal-rat-liver serum did not stain the hepatic parenchymal cell when 3'-DAB had been given 48 hr. previously. The antiserum against 3'-DAB-treated rat liver stained 3'-DAB-treated liver hepatic cells and Kupffer cells 48 hr. after admin. of 3'-DAB, but did not stain normal liver parenchymal cells. Ten mg (protein) of the microsomal fraction of normal rat liver or 3'-DAB-treated rat liver could absorb out the staining capacity of 1 ml of their respective antisera, whereas if these were cross-matched the staining capacity was unaffected. These results indicate that 3'-DAB acts as a hapten during its binding with specific proteins of hepatic cells and changes the specificity of liver specific antigen.

64-644 HISTOGENESIS OF EXPERIMENTAL TUMORS OF SOMATIC MUSCULATURE. (Rus.) Klishov,

A. A. (Dept. Histol. Embryol., S. M. Kirov Military Acad. Med., Leningrad). Ark. Anat. 45(11):102-110, 1963.

Single inj. of 3,4-benzpyrene (2 mg in 0.2 ml of sunflower oil, i.m.) to white mice resulted in rhabdomyoblastoma in 4/97 examined, and in premalignant changes in many of the mice treated. The highest degree of dedifferentiation of the muscle structure was observed between days 5-10. Somewhat later, about the area where the inj. carcinogen was localized, there was formation of a connective tissue capsule with predominance of fibroblasts and histiocytes in it; this capsule retarded the absorption of the inj. material. The myeloblasts within the capsule underwent dedifferentiation toward malignancy. Simultaneously, their metabolism was markedly increased, as indicated by the increase in RNA and in karyoplasm. In cases of rhabdomyoblastoma the myeloblasts were of different sizes and showed different degrees of dedifferentiation. However, in the process of malignant change the muscular elements have retained some normal characteristics: appearance of smooth and transverse striated myofibrils, development of symplasmatic structure and formation of primary sarcolemma.

The muscular tumor elements were in close connection not only with the blood and lymph systems but also with connective tissue stroma. The development of the muscular elements of the tumor are controlled by the same principles which govern normal histogenesis (determination, heterochromia, integration), however, in the case of the tumor, they are not fully manifested.

64-645 BIOLOGIC ASPECTS OF TISSUE GROWTH AND REGENERATION. (Fr.) Laquerrière, R.

(Dept. Pathol. Anat., Natl. Sch. Med., City Hosp., Rouen, France) and R. Laumonier. Path. Biol. (Paris) 12(1-2):14-23, 1964.

In both adult, male Wistar rats and mice of an unspecified strain, following two-thirds hepatectomy, nuclear DNase activity in the remaining hepatic tissue increased progressively from day 1-4 (max. increase of 50% on day 4) and returned to normal by day 8. These changes were accompanied by increased DNA synthesis, markedly increased by day 4, and by gradual disappearance of diploid nuclei by day 9, at which time DNA synthesis was intense. At this time 4N and 8N nuclei were predominant, and some 16N nuclei were in evidence. Similar changes in RNase activity, accompanying increased RNA synthesis, began on day 3, with return to normal values by day 7; at which time RNA activity was max. Summing up, RNA synthesis was delayed 24 hr. as compared to DNA synthesis; increased DNase activity appeared earlier, was of greater intensity and of longer duration than RNase activity. Alkaline phosphomonoesterase activity was increased only on days 2 and 3; while acid phosphatase activity in the cytoplasm reached a max. on day 4, accompanied by nuclear deprivation. 5' Nucleotidase activity, however, increased from day 2 and did not return to normal until day 8. Normal rats in parabiosis with hepatectomized animals, or receiving transfusions from the latter, showed identical DNA, RNA, and enzymatic changes, as well as identical changes of ploidy, in the hepatocytes: this appears to confirm the presence of some specific growth-stimulating substance in the plasma of the hepatectomized rats. All of these changes, in turn, were also induced in normal animals of the same strain by transfusions of plasma derived from animals undergoing carcinogenesis in response to benzidine, toluidine, or β -naphthylamine. During hepatic regeneration, the mitotic index was increased, with significantly increased DNA and RNA activity in the corneal epithelium of the salivary and lachrymal glands, the skin, and the submaxillary gland (but not in the kidney, lymphatic system, or nervous tissue). There follows a discussion (4 references) on the relationship between tumor growth and hepatectomy.

64-646 SPONTANEOUS REGRESSION OF AN INFILTRATING, METASTASIZING, EPITHELIAL TUMOR IN TRITURUS CRISTATUS IN RELATION TO THE SITE OF

INDUCTION AND POSITION IN THE SEASONAL CYCLE.

(er.) Seilern-Anspang, F. (Austrian Inst. Cancer Res., Vienna) and K. Kratochwil. Arch. Schwulstforsch. 21(4):292-300, 1963.

en tumors were induced in salamanders (Triturus cristatus) by s.c. inj. of benzpyrene, methylcholanthrene or dibenzanthracene (in olive oil), the percentage of takes, manner of tumor development, and incidence of spontaneous regression were found to depend upon the age of the animals, the season of the yr., and the inj. site. Immature animals were more susceptible to tumor take (9% of the young and 10% of the adult animals developed tumors) and showed fewer spontaneous regressions. Hibernating animals developed tumors more readily than animals inoc. in the spring or fall. In mature animals, body tumors were invariably fatal in the winter; never fatal in the spring. Tail tumors were rarely infiltrative; body tumors, almost always so. Tail tumors almost always were differentiated; body tumors, only in the spring, when the animals were sexually active. In all groups, an increased percentage tumor takes was accompanied by decreased capacity for differentiation. The authors speculate that the ability of tail tissues to regenerate a tail may be related to the increased capacity for tumor differentiation in this area and that these are related to the proportion of connective tissue in the area.

647 THE EFFECT OF CARCINOGENIC HYDROCARBONS ON GROWTH OF MICE. (E.) Rigdon, R. H. and Branch, U. Texas, Galveston) and N. J. Lunikos. Arch. Path. 77(2):198-204, 1964.

White albino mice fed laboratory chow + 3,4-benzene (BP) ad libitum showed wt. curves similar to those of controls after 0.25 and 1 mg BP/g of food and no gain in wt. after 5 mg BP/g of food. Mice fed regular chow + methylcholanthrene (MC; 5 mg/g of food) ate and weighed less than mice fed chow + pyrene (P) or anthracene (A) in doses of 25 mg/g of food. A-fed mice ate more than controls and showed wt. gains. Mice fed MC (5 mg/g of food) showed progressive decreases in the amount of food consumed and in body wt., responding to increasing conc. of MC. Addition of methionine did not prevent wt. loss. These results are explained on the basis of decreased food intake, since mice fed restricted diets also weighed less than those fed the same diet ad libitum.

48 INFLUENCE OF SEX HORMONES ON BROWN-PEARCE TUMOR METASTASIZATION. (Rus.) Grigodova, V. D. (Herzen State Oncol. Inst., Moscow). Vop. Onkol. 10(2):105-108, 1964.

Testosterone propionate (T; 10 mg x 3/wk. i.m.) or oestrol (S; 1 mg x 3/wk. i.m.) or both (each on different days) were admin. to male rats, 2-2.5 kg, 2 wk. before and 3 wk. after

inoc. of Brown-Pearce carcinoma into the left adrenal. All the animals developed tumors. Metastases occurred in 19/21 treated with T; in 18/20 treated with S; in 21/22 treated with T + S; and in 20/22 untreated controls. It is concluded that T alone or in combination with S does not significantly influence the number of metastases from Brown-Pearce carcinoma, while S increases it somewhat, when compared to controls. The hormonal effect on the metastases from the Brown-Pearce tumor depends on the site of the primary tumor.

64-649 ANTIBODIES TO THE SPECIFIC ANTIGEN OF THE TUMOR CELL MEMBRANE. (Rus.) Brondz, B. D. (N. F. Gamaleya Inst. Epidemiol. Microbiol., Moscow). Vop. Onkol. 10(2):81-88, 1964.

Heterologous sera obtained from rabbits that were immunized with 6-7 i.p. inj. of: (1) benzpyrene-induced sarcoma Sa 1 (Strain A mice); (2) methylcholanthrene (or 9,10-dimethyl-1,2-benzanthracene)-induced sarcoma MX 2 (mice of various strains), and inactivated with RBC or normal organs of mice of the same line, were able to agglutinate specific tumor antigens within the cell membranes of the above tumors which were absent in the normal tissues of these animals. Antibodies to these antigens are formed only when the immunization is made with whole cells or tumor slices, and were absent when immunized with aqueous tumor extracts. The antigens present appear to be tumor specific.

64-650 EPIDERMIS REACTION TO THE PRIMARY AND SECONDARY ACTION OF 9,10-DIMETHYL-1,2-BENZANTHRACENE ON THE SKIN OF MICE. (Rus.) Pan, C.-L. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci., Moscow). Vop. Onkol. 10(2):88-90, 1964.

Two local applications to the skin of C57BL male mice of 3% 9,10-dimethyl-1,2-benzanthracene (DMBA; in acetone) resulted in necrosis which was greater in mice pre-treated with 10-30 applications of 0.05% DMBA than in animals pre-treated with acetone only. However, the necrosis was less in those which received 20 applications of the 0.05% soln. than in those which received 30 such applications; the latter showed little evidence of necrotic change. Morphologically, 10 applications resulted in characteristic hyperplasia of the epidermis, 20 applications in papillomas and after 30 applications (besides papillomas) there were some planocellular cancers. It is concluded that at different stages of carcinogenesis the epithelium, as compared to that in normal skin, becomes less sensitive to the necrotizing effect of DMBA.

64-651 EXPERIMENTAL INDUCTION OF HEPATIC CANCER. HISTOCHEMISTRY. (Fr., Abstract) Desmet, V. and J. Vandenbroucke. Arch. Mal. Appar. Dig. 52(12):1218-1219, 1963.

The histomorphologic and histochemical study of the different stages of hepatic carcinogenesis induced in rats by 3'-methyl-4-dimethylaminoazobenzene shows that the different types of primary liver tumors arise from the same cellular line, the small undifferentiated cholangiocytic cells which line the terminal network of the intrahepatic biliary tract. The intense proliferation of these cells results in the production of the characteristic oval cells which appear about 2 wk. after the admin. of the carcinogen. The latter cells will later differentiate either into hepatocytes with the production of hepatoma or into cells of the biliary type forming adenocarcinomas.

- 64-652 SOME CYTOLOGIC CHARACTERISTICS OF EXPERIMENTAL HEPATOMAS. (Fr.)
Zajdela, F. (Curie Inst., Paris). *Arch. Mal. Appar. Dig.* 52(12):1213-1217, 1963.

In two ascites hepatomas induced in rats by feeding with dimethylaminoazobenzene, tumor cells with aberrant nuclear types were found to be capable of dividing for several generations. That these cells were alive was also shown by their capacity to synthesize proteins and RNA from radioactive precursors. The observation that the cells of a clone with homogeneous karyotype presented an homogeneous phenotypic behavior (cytoplasmic basophilia, protein and RNA synthesis) and that the heterogeneity of cytoplasmic functions within the cells of the same clone was consistently associated with nuclear heterogeneity, confirmed the importance of the nucleus in the metabolic activities of differentiated cells. However, despite the nucleus-conditioned metabolic differences, the hepatoma cells maintained the general characteristics of hepatic cells (presenting a well differentiated biliary pole as detected by the ATP-ase reaction), thus indicating that a large number of chromosomal sites of the cell-source of hepatoma are not involved in the transmission of the characters determining its status as a hepatocyte. The intense metabolic activity seen in the nucleoli of the hepatoma cells represented one of the main differences with respect to normal hepatic cells.

- 64-653 FILTERING POWER OF SOME TYPES OF CIGARETTE FILTERS. (It.) Candelì, A. (Inst. Hygiene, U. Perugia, Italy), G. Scassellati Sforzolini and N. Cusma. *Boll. Soc. Ital. Biol. Sper.* 39(18):1010-1014, 1963.

The total tar and nicotine content of smoke of "Nazionali Esportazione" cigarettes was 21.68 and 0.86 mg/cigarette, resp. These values were in the same order of magnitude of those found in several other types of cigarettes. The incorporation of a filter-tip in cigarettes afforded the best protection and reduced the amount of tar and nicotine inhaled, 51.28% and 45.3%, resp.

The filtering power of cigarette holders (based on 150 cigarettes) varied with the type of filter they contained. Type 1 (polyurethane synthetic resin) filter showed a reduction of 7.68% and 14.52% for tar and nicotine, resp., and was effective only between the 50th and 100th cigarette; Type 2 (activated charcoal and silicon) gave tar and nicotine reductions of 51.52 and 46.93%, resp.

- 64-654 SELECTIVE PRODUCTION OF BRAIN TUMORS IN RATS BY METHYLNITROSOUREA. (Ger.)
Druckrey, H. (Clin. Surg., U. Freiburg i. Br., Germany), S. Ivankovic and R. Preussmann. *Naturwissenschaften* 51(6):144, 1964.

In preliminary studies, regular i.v. admin. to BDII rats of methylnitrosourea (NU) produced after 8 mo. paralysis in 12/23 rats; in 2 of the longest survivors an ependymoblastoma and an intracerebral (IC) sarcoma were found. After 5 mg/kg i.v. (about 5% of the LD₅₀) every wk. there were 2/9 deaths from uterine sarcoma. The 7 survivors became apathic after 240 days followed by further deterioration and death 3-4 days later. Tumors found included 3 oligodendrogliomas, 2 gliomas, 1 medulloblastoma and 2 IC sarcomas (1 with a double tumor). In a second series, among 12/15 survivors there were 9 cerebral and 4 spinal tumors (1 rat with 2 tumors). In a third series 14/18 developed brain tumors; in addition there were 2 nephroblastomas, 3 uterine sarcomas, 3 mammary cancers, a squamous epithelial carcinoma of the parotid gland and one of the forestomach. While oral admin. produced mostly cancer of the stomach, i.v. admin. led to cerebral and spinal tumors. After i.v. admin. NU also resulted in carcinoma of the lungs, showing that the apparent "organotropic" specificity of the molecule relates to the whole molecule, since both substances form diazomethane in the body. (See also CRA 2(4): #655, 1964.)

- 64-655 MORPHOLOGY OF CEREBRAL TUMORS OF RATS INDUCED BY METHYLNITROSOUREA. (Ger.)
Thomas, C. (Inst. Pathol. Neuropath., U. Bonn, Germany) and G. Kersting. *Naturwissenschaften* 51(6):144-145, 1964.

Of 32 tumor-bearing rats as a result of i.v. methylnitrosourea admin. (please see preceding abstract) 30 had cerebral tumors (3 with simultaneous spinal cord tumors), and 2 with only spinal cord tumors. The cord tumors included a neuroinoma, a caudal ependymoma and an intramedullary spongioblastoma. Two of the 30 intracranial tumors were extracerebral. One of them arose 312 days after a single inj. of 100 mg/kg and was similar to tumors obtained with 2-acetylaminofluorene. Both were primary neuroectodermal tumors and included some well preserved nervous tissue of the Gasserian ganglion. The intracerebral tumors were 7/28 isomorphic gliomas, 7/28 polymorphic gliomas, 11/28 mixed tumors with

ial tissue including sarcomatous foci (one s.c. motransplanted specimen produced an extensive indle cell sarcoma); the 3 rats which also had inal cord tumors gave the picture of diffuse rebral reticulosarcomas.

-656 ON THE IN VIVO PROTEIN BINDING OF 1-HYDROXY-2-ACETYLAMINOFLUORENE-1-4 IN THE RAT. (E.) Irving, C. C. (VA Med. aching Group Hosp., Memphis, Tenn.) and R. F. illiard. *Cancer Res.* 24(1):77-82, 1964.

ly 1-2% of a single dose of 3-4 mg of 1-hydroxy-acetylaminofluorene-1- C^{14} (1-hydroxy-AAF-1- C^{14} ; spended in 1 ml of 7% gum acacia in 0.9% saline; min. i.p., s.c. or by oral intubation) remains the tissue of male albino rats 24 hr. after min. Radioactivity equivalents (μ moles of hydroxy-AAF-1- C^{14} /g protein) bound to tissue proteins were: 15-19 in liver, lung and plasma; n kidney; and 0.1-5 in the g.i. tract, heart, een, bladder and brain. These values remained stant 12-48 hr. after dosage and were unaltered varying the route of admin. Comparative dies of i.p. inj. showed tissue proteins to e a far greater affinity for 2-acetylmino-orene-9- C^{14} .

657 METABOLIC REGULATORY CIRCUITS AND CARCINOGENESIS. (E.) Pitot, H. C. Ardle Mem. Lab., U. Wisconsin Sch. Med., ison) and C. Heidelberger. *Cancer Res.* 10):1694-1700, 1963.

authors present alternative explanations, ed upon present concepts of metabolic regula- n and control, that permit the perpetuation of abolic changes brought about by the temporary eraction of the carcinogen and a cytoplasmic tein, not necessarily as a consequence of ect interaction of the carcinogen with genetic erial. In one modified product perpetuation uit, the protein to which the carcinogen is d ls the repressor of the growth process; s repressor is deleted in the cancer cells this deletion does not depend on the con- ed presence of the carcinogen in the daughter s. In another modification (product inde- ent circuit), the product of the catalyzed ction does not enter into the regulatory cir- t. Thus, if malignancy is not the result of rect gene (DNA) mutation, a reversion from malignant to the nonmalignant state is well in reason.

58 THE CHROMOSOMES OF THE 7,12-DIMETHYL- BENZ(A)ANTHRACENE-INDUCED TUMORS IN OMYS. (E.) Huang, C. C. (Roswell Park Mem. ., Springville, N. Y.) and L. C. Strong. *er Res.* 23(11):1800-1807, 1963.

chromosome constitution of 10 primary tumors ced by 9,10-dimethyl-1,2-benzanthracene

(DMBA; s.c. inj. of 0.1 ml of 1% soln. in olive oil) and four of their early transplant lines in 8-mo.-1-year-old mice, both sexes, of *Mastomys coucha* was investigated. In a total of 326 cells examined, 85.3% contained the normal diploid chromosome number of 36, 11.3% contained from 34-38 and 3.4% contained from 63-140 \pm 1 chromo- somes. The tumors studied were individually dif- ferent from one another. Four primary tumors had a normal diploid mode, but with structural de- partures from the normal karyotype; one primary tumor had a mode of 36 + one minute with a low frequency of cells between the range of 63 and 77 plus one to four minute chromosomes; 5 primary tumors had widely distributed chromosomal modes from hypotetraploid to hypertetraploid. Chromo- some breaks were observed in 4 primary tumors, but no clear pattern was found with regard to the num- ber of breaks/cell or the chromosomes in the com- plement involved. Two transplanted *Mastomys* tumor lines maintained the same chromosome pattern as was observed in their primary tumors. In two other tumor lines, one shifted from a tetraploid to a hyperdiploid mode in the sixth transfer generation, the other from diploid to hypertetra- ploid in the first transplant generation.

64-659 THE EFFECT OF GONADECTOMY ON THE EXPERIMENTAL PRODUCTION OF BLADDER CARCINOMA IN THE FISCHER RAT (F/Fu). (E.) Veenema, R. J. (Inst. Cancer Res., Francis Delafield Hosp., New York), B. Fingerhut and M. Tannenbaum. *Invest. Urol.* 1(6):587-592, 1964.

Fischer 344 (F/Fu) rats (2-month-old) fed a carcinogenic diet low in vitamin B6 and containing 2-fluorenylacetamide (600 mg/kg) were divided into the following groups: Group I, oophorecto- mized (2 wk. previously) female rats fed the diet; Group II, orchiectomized (orx.) rats fed the diet; Group III, orx. rats implanted s.c. with diethyl- stilbestrol (10 mg) and fed the diet; Group IV, intact female rats fed the diet. Group I and IV animals showed bladder hyperplasia within 6-8 mo. of age and well differentiated papillary (papil- lomas) tumors in 4/12 and 3/12, resp., as well as carcinomas of the bladder in 4/12 and 5/12 within 7-11 mo.; squamous changes were seen when the tumors were permitted to develop longer than 10 mo. In Groups II and III, no bladder tumors developed but hyperplasia was seen in 6/9 and 1/4, resp., and papillomas in 3/9 and 3/4 within less than 4-10 mo. All the animals had high incidence of liver toxicity consisting of cystadenomas and to a lesser degree of liver fibrotic changes or hepatoma. Another group of orx. rats were placed on the diet immediately after castration but all the animals died within 1-2 mo. with contracted bladders and hyperplastic bladder mucosa; the early mortality may have been due to the young age of the animals. (See also CRA 2(2):#255, 1964.)

64-660 PULMONARY RETICULOENDOTHELIOSIS FOLLOW- ING INHALATION OF HAIR SPRAY. AN

EXPERIMENTAL STUDY. (Sp.) Doyle, J. A., M. Golonbek and M. R. De Ramirez. *Arch. Histol. Norm. Pat.* 8(3):290-296, 1963.

Histologic examination of the lungs of an adult male guinea pig, after forced inhalation of air saturated with hair spray for 2-3 days, showed the following: presence of PAS-positive particles in all sections of the lung; hyperplasia and hypertrophy of the RES with tendency toward granuloma formation; phagocytosis of particles by macrophages.

64-661 MAMMARY AND PERITONEAL TUMORS INDUCED BY INTRAPERITONEAL ADMINISTRATION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE IN NEWBORN AND ADULT RATS. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.) and R. Fukunishi. *Cancer Res.* 23(5):785-789, 1963.

When 50-day-old female Sprague-Dawley (S-D) rats were given a single i.p. inj. of a lipid emulsion of 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.5-20 mg) with sacrifice at 180 days, all the rats admin. 5-20 mg developed mammary cancer within 60 days, while those admin. 2.5 mg developed mammary cancer at a slower rate. Ear tumors and sarcoma at the inj. site also occurred in a few animals. A sterile compressed pellet of DMBA (13.7-21.6 mg) was deposited for 7 mo. in the peritoneal cavity of 50-day-old female S-D rats; peritoneal tumors occurred in 14/17 (82.3%) rats, of which 11 were spindle cell sarcomas and 3 were mesotheliomas; 2/14 also developed mammary cancer 37 or 57 days after implantation. A single i.p. inj. of DMBA (0.25 mg) in newborn S-D or Long-Evans (L-E) female rats caused the following tumor incidence: 53.3% and 5.1% mammary carcinomas; 74.4% mammary fibroadenomas; and 6.6% and 0% ear tumors, resp. In similarly treated S-D and L-E newborn males, no carcinomas were found in either strain, while 16.7% and 1.9% developed mammary fibroadenomas and 27.8% and 3.7% ear tumors, resp. Of the 12 rats with fibroadenoma, 6 also had mammary carcinoma, while the male and female L-E rats developed 3 renal adenocarcinomas and 2 leukemias. Runt disease was induced in some of the newborn rats. (See also CRA 1(5):#878, 1963.)

64-662 EXFOLIATIVE CYTOLOGY IN EXPERIMENTAL ORAL CARCINOGENESIS. (E.) Camilleri, G. E. (Dept. Dent. Sci., Royal Coll. Surg. Eng., Lincoln's Inn Fields, London, W.C.2) and C. J. Smith. *Acta Cytol. (Baltimore)* 8(1):85-90, 1964.

The left cheeks of Syrian hamsters (approx. 10 wk. old) were painted with 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.5% in liquid paraffin solns. 3x/wk.). Exfoliative smears from untreated and paraffin oil-treated groups were essentially similar. At 2-4 wk., smears of DMBA-treated animals showed a dense collection of inflammatory cells, which had returned to normal by wk. 5-8.

At 8-9 wk., smear studies showed many inflammatory cells, a predominance of nucleated epithelial cells, and cells (with nuclei filling almost the whole of the cell) which were regular at first but which gradually became indicative of malignancy. Histological studies during this period showed epithelial hyperplasia and dyskeratosis. By wk. 14, the hamsters developed rapidly growing tumors with clinical and histologic signs of malignancy. Smears showed the presence of two main cell types (one whose nucleocytoplasmic ratio was markedly altered in favor of the nucleus; a smaller one with cyanophilic cytoplasm and irregular, hyperchromatic, nucleus) satisfying the criteria for malignancy. By wk. 16, the tumors were large, grossly infected and bled profusely when scraped.

64-663 HISTOGENESIS AND PATHOGENESIS OF EXPERIMENTAL CARCINOMA OF THE UTERINE CERVIX. (E.) Wolfson, N. I. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad). *Acta Un. Int. Cancr.* 19(3-4):678-679, 1963.

In virgin female mice (line A or D; 1.5-4.5 mo. old), cervical or vaginal carcinomas were induced by 15-35 local applications of 9,10-dimethyl-1,2-benzanthracene (DMBA; 1 mg, paraffin pellets placed in the cervical canal; or 0.075 mg in ethylene-glycol suspension on cotton tampons; or 0.0075-0.015 mg on sponge tampons intravaginally 1-2/wk.). Epithelial changes in the cervix uteri or vagina occurred in 98%, regardless of the route of admin.; cancers and benign tumors (3:1) were seen in 75%. These cancers in 50% of the cases were composed of bifunctional epithelium; others were squamous cell (cornified or noncornified) carcinoma. Vaginal papillomas following admin. of ethylene-glycol alone were seen in 3/22 cases; addition of testosterone propionate (TP, dose not specified) delayed tumor appearance (8/21) 6-7 mo. Addition of TP (0.045 mg) to DMBA decreased the incidence of cancer, but increased the incidence of precancerous lesions.

64-664 CHANGES IN PROTEIN AND RIBONUCLEIC ACID METABOLISM IN HEPATIC EPITHELIAL CELLS DURING EXPERIMENTAL CARCINOGENESIS BY DIETHYLNITROSAMINE. (Ger.) Oehlert, W. (Inst. Path., U. Freiburg i. Br., Germany) and J. Hartje. *Beitr. Path. Anat.* 128(3):376-415, 1963.

A more detailed summary of studies reported previously as CRA 1(4):#660, 1963, adds that protein synthesis (as measured by the H³-leucine uptake by cell protein) was particularly strongly depressed in the centrilobular hepatic epithelium prior to the appearance of hepatomas in mature, male albino rats fed diethylnitrosamine (5 mg/kg/day for 120-150 days, in drinking water), while RNA synthesis was heightened in the nuclei of both central and peripheral cells. Prior to the appearance of the tumor, RNA synthesis was most markedly elevated in highly vacuolated columns of cells with enlarged nuclei and nucleoli, found at

the center of the lobule. The relative rate of RNA synthesis (corrected to account for the surface area of the nucleus) increased progressively during the entire period of carcinogenesis with peaks in "microcarcinomata" and in fully developed tumors. There was a simultaneous, progressive reduction of cytoplasmic RNA content in these tumor cells during the period of carcinogenesis, while in fully developed carcinoma cells, cytoplasmic RNA content and the rate of RNA synthesis in the nucleus were both significantly increased over normal values. The authors conclude that an essential factor in the transformation of normal liver epithelial cells into cancerous ones is a progressive conversion of cell-specific DNA.

665 CHANGES IN METABOLIC VALUES AND IN GLYCOLYTIC ENZYME ACTIVITY DURING THE INDUCTION OF CANCER IN RAT LIVERS BY MEANS OF DIETHYLNITROSAMINE. (Ger.) Heise, E. (Robert-Rössle Clin., German Acad. Sci. Berlin, Berlin) and M. Görlich. *Exp. Cell Res.* 33(1-2): 9-300, 1964.

Complementing previous studies in which rat hepatomas were induced by feeding dimethylaminobenzene (DAB; see CRA 1(4):#652; and *ibid.* (4):#879, 1963), inbred male Sprague-Dawley rats (approx. 200 g) were given 10 mg/kg/day of diethylnitrosamine in water, by gastric intubation. Liver wt. was increased by approx. 150% at the end of the 120-day period of carcinogenesis, in contrast to an increase of approx. 50% in the presence of DAB-induced hepatomas. Liver slices and homogenates obtained at 20-day intervals, no significant changes in O_2 partial pressure were observed; however, aerobic glycolysis was tripled by day 60 and continued at that level thereafter. (An increase of aerobic glycolysis began to be evidenced by day 40, although macroscopic evidence of tumefaction was still lacking at that time.) In liver slices, significant increase of anaerobic glycolysis was seen from day 100 on. Similar changes of aerobic glycolytic activity were not demonstrable in liver homogenates. Studies of total liver activity, compensated for changes in liver size and wt., confirmed that the process of carcinogenesis took place in irregular "spurts," rather than as a gradual progression; with FDPase activity falling off sharply from day 50 on, to reach a final plateau level of approx. one-third the initial values by day 110, while G6Pase activity only declined to 65% of original values before reaching a final plateau on day 90. In all cases, the overall tendency to decline was interrupted periodically by periods of plateau of slight, transient increase of activity. In comparing these data with those derived from rats with DAB-induced hepatomas, the authors conclude that a positive correlation exists between the degree of changes seen in FDPase and G6Pase activity and the degree of malignancy of the hepatic tumor.

64-666 RHO-SIGMA-PI ANALYSIS. A METHOD FOR THE CORRELATION OF BIOLOGICAL ACTIVITY AND CHEMICAL STRUCTURE. (E.) Hansch, C. (Dept. Chem., Pomona Coll., Claremont, Cal.) and T. Fujita. *J. Am. Chem. Soc.* 86(8):1616-1626, 1964.

The effect of varying the substituents in extensive series of dimethylaminoazobenzenes, benzanthracenes, benzacridines and other aromatic hydrocarbons was subjected to regression analysis, using published data on the carcinogenic activity of these compounds in mice. While results from the rho-sigma-pi analysis with carcinogenic hydrocarbons were not as sharp as those found for other systems, they are convincing enough to show that the lipophilic character of these molecules must be considered in attempts to rationalize structure-activity relationships.

64-667 SUSCEPTIBILITY OF STRAIN B6AF₁/J HYBRID INFANT MICE TO TUMORIGENESIS WITH 1,2-BENZANTHRACENE, DEOXYCHOLIC ACID, AND 3-METHYLCHOLANTHRENE. (E.) Klein, M. (Dept. Anat., U. Tennessee Med. Units, Memphis). *Cancer Res.* 23(10):1701-1707, 1963.

Male 7-8-day-old B6AF₁/J mice were given 15 inj. by stomach tube of 1,2-benzanthracene (BA), deoxycholic acid (DC), or 20-methylcholanthrene (MC), each 3% suspended in 0.1% methocel-Aerosol O.T. (dioctyl ester of sodium sulfo-succinic acid) with sacrifice at the median age of 340-444 days (Group I) or 547-600 days (Group II). Of the animals in Group I, the treatments produced the following incidence (in percent) of hepatomas, pulmonary adenomas, lymphocytic neoplasms, reticulum-cell neoplasms Type A, forestomach papillomas, and large intestine adenocarcinomas: BA, 46%, 95%, 0%, 3%, 5%, and 0%; DC, 0%, 10%, 0%, 0%, 0%, and 0%; MC, 49%, 100%, 11%, 0%, 53%, and 6%; solvent only, 0%, 26%, 0%, 3%, 0%, and 0%; untreated controls, 0%, 10%, 0%, 0%, 0%, and 0%, resp. In Group II, the treatments produced the following incidence of hepatomas, pulmonary adenomas and lymphocytic neoplasms (the other tumors above did not develop): BA, 100%, 95% and 0%; DC, 16%, 37% and 0%; solvent only, 10%, 35% and 10%; untreated controls, 10%, 30% and 10%, resp. When another group of mice were admin. only 2 doses of 3% BA with sacrifice at 568 days of age, the incidence of hepatomas and pulmonary adenomas was 80% and 85%, resp.; the other tumors did not occur. It was noted by the author that the high carcinogenic effect of BA was not due to an impurity.

64-668 A SULPHONAMIDE DERIVATIVE WHICH INDUCES URINARY TRACT EPITHELIAL HYPERPLASIA AND CARCINOMAS OF THE BLADDER EPITHELIUM IN THE MOUSE. (E.) Bonser, G. M. (Dept. Exptl. Path., U. Leeds Sch. Med., England) and D. B. Clayson. *Brit. J. Urol.* 36(1):26-34, 1964.

Addition of 4-ethylsulfonylnaphthalene-1-sulfonamide

(hyperplastic agent, HPA; 0.01%) to the diets of 65 Ab x IF hybrid mice of both sexes (killed when moribund or at 65 wk.) gave the following results: survival of 28/65 mice for 30 wk. and of 14/65 mice for 65 wk.; appearance of first carcinoma after wk. 33; carcinoma of the bladder in 10 mice (36%); coexistence of papillomas and carcinomas in many bladders. Female mice appeared more susceptible than males (9/16 bladder carcinomas as compared to 1/12). Previous treatment of HPA-fed mice with a single dose of 9,10-dimethyl-1,2-benzanthracene (DMBA; 2.5 mg oil, intragastric) did not alter the results: survival of 36/53 mice for 30 wk. and of 13/53 mice for 65 wk.; 8 mice with carcinomas of the bladder. The hyperplastic effect of HPA has been shown to be apparent as early as 2 days after the start of treatment and to be induced by conc. as low as 0.0025%. Of 9 strains tested, Strains WLL, Strong A, Ab x IF, C57 x IF and Tuck proved sensitive. In tests with HPA analogs, slight modifications of the alkylsulfonyl group did not destroy the hyperplastic activity, while this activity was usually destroyed by variation of the alkylsulfonyl and sulfonamide groups on the naphthalene ring. Most of the analogs were inactive.

- 64-669 CHANGES IN RESPIRATORY EPITHELIUM INDUCED BY SINGLE LARGE APPLICATION OF TOBACCO TAR: AN EXPERIMENTAL STUDY IN DOGS. (E.) Greenberg, S. D. (Dept. Path., Baylor U. Coll. Med., Houston, Tex.) and G. L. Hallman. Southern Med. J. 57(4):417-422, 1964.

To observe the effect of a single large application of crude tobacco tar on the respiratory epithelium, a Gelfoam pledget (0.5 cm in diameter and saturated with 0.3 ml of crude tobacco tar) was inserted into the isolated distal upper right lobe bronchus of the dog. The bronchus was then closed and the dogs were killed 2, 4, 6 wk. and 2, 6, 8, 10, and 12 mo. after the operation. In controls receiving the surgical technic without application of tobacco tar, although all terminal air spaces were collapsed, the normally thin-walled septa and respiratory epithelium were intact and no inflammatory changes were seen. In the study group, a single large application of tobacco tar produced necrosis of the epithelium, lamina propria and bronchial cartilage. Areas of basal cell hyperplasia, but no atypical change or carcinoma, were seen 2 and 4 wk. later. By wk. 6 the tobacco tar had left the bronchial lumen and was seen within macrophages in the bronchial wall and lymph nodes; partial regeneration of the respiratory epithelium occurred. At 2 mo., respiratory epithelium was completely regenerated and necrotic areas remained only in the bronchial cartilage. In the present study bronchogenic carcinoma was not produced by single, large applications of tobacco tar.

- 64-670 THE METABOLISM AND POSSIBLE MODE OF ACTION OF URETHANE. (E.) Boyland, E.

(Chester Beatty Res. Inst., Royal Cancer Hosp., London, S.W. 3), R. Nery, K. S. Pegg and K. Williams. Biochem. J. 89(3):113P-114P, 1963.

After a brief review (8 references) of the biological effects and metabolism of urethan (U) in rats, rabbits and man, it is noted that 10⁻² M N-hydroxyurethan (NOHU) caused chromosome breakage in the root tips of *Vicia faba* whereas 10⁻² M U did not. Also, U reacted slowly with the SH group of glutathione in the presence of rat liver suspensions whereas NOHU reacted with glutathione in the absence of rat liver suspensions to give a product with properties similar to those of S-ethylglutathione; this suggests that the biologically active NOHU, to which animals, but not plants, can convert U, may be the active metabolite responsible for the radiomimetic effects of U when admin. to animals, although some simple hydroxylamine released in the tissue may be responsible.

- 64-671 CARCINOGENIC LACTONES AND RELATED SUBSTANCES. (E.) Dickens, F. (Middlesex Hosp. Sch. Med., London). Brit. Med. Bull. 20(2):96-101, 1964.

After a review (44 references) of pertinent literature and his own earlier work, the author reports tests in progress (52 wks.) which showed no carcinogenic effects from α,β -dimethylmaleic anhydride, N-ethylmaleimide or saturated succinic anhydride. Two of 5 rats injected with phenyl vinyl ketone were currently developing tumors. (See also CRA 1(1):#72; ibid., (5):872, 1963 and ibid., 2(3):#484, 1964.)

- 64-672 CHROMOSOME STUDIES IN NORMAL AND LEUKEMIC RATS. (E.) Dowd, G. (Holy Ghost Hosp., Cambridge, Mass.), K. Dunn and W. C. Moloney. Blood 23(5):564-571, 1964.

At the age of 3 mo., two groups of non-inbred Wistar and inbred Wistar/Furth rats were exposed to total body X-irradiation (430 rads; 30-32 rads/min.) or were treated with 20-methylcholanthrene (MC; 10 mg/day, total 180 mg, intragastric). A small group was first irradiated, then given 180 mg of MC after 6 mo. Chromosome preparations, using the modified Moorhead technic, were obtained in 70% of normal rat peripheral blood cells; culture preparations from blood of leukemic rats were generally unsuccessful. Adequate metaphase preparations were obtained from the bone marrow of 8 leukemic rats (7/8 pretreated with X-ray, 1/8 with X-ray + MC). No consistent chromosome abnormalities, such as those reported in human myeloid leukemia, were found among these leukemic rats.

- 64-673 ANESTHETIC EFFECT ON PULMONARY METASTASES IN RATS. DEVELOPMENT OF METASTASES OF WALKER 256 CARCINOSARCOMA. (E.) Agostino, D.

loan-Kettering Inst. Cancer Res., New York)
d E. E. Clifton. Arch. Surg. (Chicago)
(5):735-739, 1964.

oculation of 1 ml of Walker 256 carcinosarcoma
11 suspension (25,000 cells in ascitic fluid)
to adult Wistar female rats (av. wt. 200 g)
ve the following results at death or after 9
: 64% lung metastases after anesthesia with
oroform; 55% with ether; 46% with i.p. pento-
bital sodium (Nembutal); 37% in controls
ceiving no anesthetic. Changes in blood clotting
hanism are considered as a possible explana-
n for the increase in pulmonary metastases
er admin. of certain anesthetics.

674 BENZOPYRENE-INDUCED TUMOURS IN THE
CLAWED TOAD, XENOPUS LAEVIS. (E.)
ls, M. (Dept. Exptl. Zool., U. Geneva,
tzerland). Experientia 20(3):143-145, 1964.

adult anurans (X. laevis laevis) implantation
benzopyrene crystals (BP; 1.5 mg in the ab-
dinal wall) produced lymphosarcomas (86-288
s later) in 11/13; metastases, particularly
the liver and spleen, appeared in 7/11. The
induced tumors histologically were similar to
ntaneous lymphoid tumors of Xenopus and to
se induced by 20-methylcholanthrene crystals.
gments of a BP-induced liver tumor transplanted
the dorsal lymph sac of 6 immature animals
ved widespread growth and metastasis to
ey, liver and spleen. Single small doses of
crystals in egg albumen were placed in the
al lymph sac or abdominal cavity of 20 im-
e animals and 9 bore lymphoid tumors of
er, kidney, spleen or abdominal wall muscle
they were killed 270-310 days later.

75 A COMPARISON OF POLYCYCLIC AROMATIC
HYDROCARBON EMISSIONS FROM DIESEL- AND
OL-POWERED VEHICLES IN PARTIALLY SEGREGATED
FIC LANES. (E.) Sullivan, J. L. (Air Pollut.
rol Branch, N.S.W. Dept. Public Health,
ey, Australia) and G. J. Cleary. Brit. J.
str. Med. 21(2):117-123, 1964.

dney, Australia, where during the evening
fic peak, diesel and gasoline powered vehicles
partially segregated, air particulate samples
collected from each lane (over a period of
) and analyzed for polycyclic aromatic hydro-
ns. The conc. in ppm of suspended matter
ected, for the diesel and gasoline-powered
s was, resp.: pyrene, 122 and 227; 1,2-benz-
racene, 32.4 and 31.2; 3,4-benzpyrene, 83.5
9.4; and 1,2-benzpyrene, 50.7 and 23.3;
-benzperylene, 88.5 and 48.0; coronene,
and 53.9. Similar "background" values
en from a point 300 yards away) were, resp.:
10.1, 14.7, 14.0, 34.1 and 33.9. Smoke
ties (weighed sample pads, mg/m³) for diesel
gasoline lanes, were, resp., 0.289 and 0.156
ground, 0.149). An association was estab-
ed between traffic containing diesel vehicles

and the conc. of smoke, 1,2-benzpyrene, 3,4-benz-
pyrene, 1,12-benzperylene and coronene.

64-676 EXPERIMENTAL CANCER OF THE PROSTATE.
(E.) Wojewski, A. (Clin. Urol.,
Pomeranian Acad. Med., Szczecin, Poland) and
A. Laska. Urol. Int. 17(4):223-229, 1964.

Adult albino rats were orchietomized 3 mo. before
20-methylcholanthrene (MC; 5 mg) inj. into the
prostate and squamous cell carcinomas of the
prostate were seen in 3/10 animals at autopsy
1 yr. after MC admin.; rats treated only with MC
(5 mg) showed 7/11 tumors, of which 1 was a
squamous cell carcinoma and the other 6 were white
cysts with a wall of fibrous connective tissue
lined with squamous epithelium with MC and caseous
content. When the rats were treated with estradiol
prolongatum (Dimenformen; 0.5 mg at 4-wk. inter-
vals) 3 mo. before MC admin., no malignant changes
were seen in the prostate, although 3/10 animals
had the cysts described above. When the rats were
treated with Sustanon 100 (presumably a mixture of
testosterone decanoate, 4-methylvalerate, propionate
and phenylpropionate; 0.05 ml at 4 wk. intervals),
1/10 developed a squamous cell carcinoma and 1/10
a sarcoma of the prostate. No animals showed
metastases.

64-677 EFFECT OF 3-METHYLCHOLANTHRENE
CRYSTALS AND SOLUTIONS ON THE CHORIO-
ALLANTOIC MEMBRANE OF THE DEVELOPING CHICK EMBRYO.
(E.) Beohar, P. C. (Dept. Path., Coll. Med.,
Jabalpur, M. P., India), P. Goldhaber and A. T.
Hertig. Indian J. Med. Res. 52(3):263-272, 1964.

After single, topical applications of 20-methyl-
cholanthrene (MC) crystals to the chorioallantois
of White Leghorn chick embryos, the survival rate
of the embryos rose steadily from 1/18 after day
5 application to 7/10 after day 10 application.
The histologic changes in 5-9-day embryos included
essentially keratogenic and prickle-cell meta-
plasia of the ectoderm, foreign-body-like granu-
lomas around MC particles in the mesenchyme and
goblet-cell formation in the allantoic endoderm.
Tenth day embryos revealed, in addition, extensive
epithelial cell migration into the mesenchyme.
Keratogenic metaplasia of varying degree was also
seen after treatment with 0.01 ml of acetone
(26/30 survived) and egg shell powder. Tests on
7-day chick embryos showed that only acetone and
polyethylene glycol (0.01 ml; each 4/6 survivals
after 18 days) were suitable to use as solvents
for MC. The survival of 10-day chick embryos
for control groups, acetone groups, groups re-
ceiving 5 µg MC in 0.01 ml acetone and groups
receiving 5 µg MC in 0.01 ml polyethylene glycol
was 100%, 83%, 0% and 58%, resp.

64-678 EVOLUTION OF SQUAMOUS CELL CARCINOMA
IN THE RAT. (E.) Zackheim, H. S.
(Dept. Derm., Wayne State U. Coll. Med., Detroit,
Mich.). Arch. Path. 77(4):434-444, 1964.

After repeated weekly applications (13-38 wk.) of 0.1 or 0.18 ml of a 0.5% soln. of 9,10-dimethyl-1,2-benzanthracene (DMBA) in acetone to the unshaved midback region of 52 rats (23 Fisher, 15 Holtzman, 14 hooded), of both sexes, the following data were recorded: 38/52 (73%) of rats developed squamous cell carcinoma of the skin with or without benign warty papules (papillomas); 5/32 (10%) had only warty papules; 9/32 (17%) had neither lesion. Basal cell tumors were found in 17/32, fibrosarcomas in 8/32, sebaceous (basal cell) epitheliomas in 1/32 and sebaceous adenomas in 2/32. The author also presents a detailed description of both early and later changes induced by DMBA admin., as well as a picture of the histologic changes accompanying the evolution of the verrucous papule.

- 64-679 THE EFFECT OF KERATOACANTHOMAS ON THE DEVELOPMENT OF SHOPE PAPILLOMAS IN THE RABBIT. (Ger.) Solomon, L. M. (Clin. Derm., U. Pennsylvania Sch. Med., Philadelphia) and H. Beerman. Hautarzt 15(2):86-87, 1964.

Female mature New Zealand white rabbits were admin. 9,10-dimethyl-1,2-benzanthracene (DMBA; 1% in lanolin and mineral oil, daily for 3-13 wk. to shaved left flank) until keratoacanthomas (1-20 tumors) developed at the application site. When the keratoacanthomas (Type 2 and 3) regressed partially (2/5) or totally (3/5), the rabbits were inj. s.c. in the right ear lobe with Shope papilloma filtrate (0.2 ml). Another group of rabbits in which keratoacanthomas were not induced received a single inj. of the papilloma filtrate s.c. in the right earlobe, followed by topical application to the flank with lanolin and mineral oil for 16 wk. In the latter group, papillomas developed at the site of inj. within 34-46 days, whereas the former group developed papillomas within 14-32 days. While contamination of the earlobes with DMBA is a possibility, the faster appearance of papillomas in the former group of rabbits shows nonetheless that DMBA works as a systemic initiating agent, and acts to depress the body's defense mechanisms.

- 64-680 EFFECTS OF DIET ON PITUITARY TUMOR INDUCTION BY ESTROGENS. (E.) Ershoff, B. J. (Western Biol. Lab., Culver City, Cal.). Exp. Med. Surg. 22(1):28-32, 1964.

Immature female Sprague-Dawley rats were fed estrogens (20 mg/kg of ration) in a stock ration, a purified diet alone or + 10% desiccated liver for 242 days; no ovarian or uterine tumors were induced by estradiol (E) feeding, while diethylstilbestrol (DES) in all the 3 diets produced ovarian and/or uterine tumors in 66% of the rats. Ethinyl estradiol (EE) added to the purified ration induced ovarian and/or uterine tumors in 10/16 of the survivors, but tumor only occurred in 2 of the animals from each group fed the liver-supplemented or stock rations. E did not affect

the pituitary wt., but DES and EE caused a marked increase in the av. pituitary wt. (37 and 34 mg, resp.; controls, 11 mg) with extensive adenomatous changes in the anterior lobe only in the animals fed the purified ration. None of the estrogens caused mammary tumors or tumors in the other tissues examined. No correlation was seen at sacrifice between the decrease in body wt. and the pituitary wt.

- 64-681 THE COAGULATION FACTOR IN THE PRODUCTION OF METASTASES. EFFECTS OF FIBRINOLYSIN AND HEPARIN. (It.) Agostino, D. (Sloan-Kettering Inst. Cancer Res., New York) and E. E. Clifton. Osped. Ital. Chir. 9(4):393-406, 1963.

In 3- and 8-week-old (wt. 30-40 and 180 g, resp.) female Wistar rats, inoc. of 100,000 Walker 256 ascitic carcinosarcoma cells into the femoral vein induced pulmonary metastases in 85% of the animals. Administration of fibrinolysin (F; 5000 U; inj. i.v. 15 min. before inoc.) reduced animals with metastases to 25%. Admin. of heparin (H; 50 U; i.v. 10 min. before inoc.) reduced the metastases to 35% (controls, 65%). Administration of coumadin ("Panwarfin"; 1.5 mg. i.v. 20 hr. before inoc.) produced metastases in 49% of rats (controls, 64%). Following inoc. of 25,000 tumor cells, pulmonary metastases developed in 34% of controls, 61% of animals rendered hyperlipemic by a special high fat diet, 72% of animals receiving 75 U and 43% of animals receiving 50 U of Trasylol ("Bayer 128"; admin. i.v. 10 min. before inoc.), and 85% of animals receiving 40 mg and 61% of the animals receiving 20 mg of epsilon aminocaproic acid (EA; admin. i.v. 10 min. before inoc.). A single dose of H or F, as above, decreased the tumor cell count in the systemic circulation significantly. In animals receiving EA or Trasylol, cancer cells disappeared from the systemic circulation entirely within 15-30 min. The subsequent transplantability of tumor cells was greatly reduced by treatment of the donor animals with H or F.

- 64-682 FUNCTION OF DEPRESSED IMMUNOLOGIC REACTIVITY DURING CARCINOGENESIS. (E.) Prehn, R. T. (Dept. Path., U. Washington, Seattle). J. Nat. Cancer Inst. 31(4):791-805, 1963.

Hybrid female mice (BALB/c female x C57BL male; 3 mo. old) were treated s.c. with 4 paraffin pellets (diameter 2 mm) containing 20% of 20-methylcholanthrene (MC); 3 wk. later, the mice were inoc. s.c. with fragments of male spleen from the same hybrid strain; 1 wk. after spleen inoc., mice received male skin grafts of the same genotype. MC pellets significantly suppressed reaction against male skin grafts. Experiments using (C57BL x C3H)F₁ hybrids (a single pellet was admin. to 1 group) and (C57BL female x BALB/c male)F₁ hybrids, with different intervals between pellet implantation and spleen inoc., gave similar results.

683 EPITHELIAL PROLIFERATION OF THE LUNG ASSOCIATED WITH CORTISONE ADMINISTRATION. PATHOLOGICAL AND EXPERIMENTAL STUDY. (E.) Markheiser, S. W. (Dept. Lab., Harrisburg Lyclyn. Hosp., Pa.). Cancer 16(10):1354-1364, 1963.

Pathologic examination of lung sections taken at autopsy from 44 pts. (25 male, 19 female; av. age 46 yr.), all of which received treatment with cortisone and/or derivatives for varying periods of time (4 days-7 yr.; 8/14 with rheumatoid arthritis, 1-7 yr.), revealed 9.1% cases with dermal metaplasia (cells analogous to those found in oat cell carcinoma), 6.8% with atypical squamous and basal cell metaplasia, and other types of bronchiolar proliferation. Of 70 female subjects treated with cortisone acetate (12.5 mg/day i.m. x 1/wk. for 4 mo.), among the progressive changes observed, epidermal metaplasia was seen in 22%, atypical nuclear forms in 20%, multiple adenomas of the adrenal cortex in 10%. It is suggested that, although many factors are probably not the immediate causative agents of lung cancer, they may modify or influence stimuli that are directly involved in the pathogenesis of cancer.

684 RELATION BETWEEN CIRRHOSIS AND TRACE METAL CONTENT OF LIVER WITH SPECIAL REFERENCE TO PRIMARY BILIARY CIRRHOSIS AND CARCINOMA. (E.) Hunt, A. H. (St. Bartholomew's Hosp., London), R. M. Parr, D. M. Taylor and G. Trott. Brit. Med. J. 2:1498-1501, 1963.

Significant reduction of liver Zn conc. (from normal value of 67 µg/g wet wt. to 40 µg/g) was found in 5 pts. with carcinoma of the liver; similar reductions were found in cirrhotic pts. Significantly increased levels of Zn were found in 10 cases of carcinoma of the stomach (136 µg/g, 0.01) and in 5 cases of leukemia (108 µg/g, 0.05). Significantly reduced levels of Co (0.01) were also found in cancer pts. The conc. of Cu in the liver of normal subjects (3.5 µg/g wet wt.) was 7; for pts. with cancer (all 12, cancer of the liver 14, Wilson's disease 128, biliary cirrhosis 220. In one pt. with obstructive jaundice due to carcinoma of pancreas Cu conc. was only 3.2 µg/g, probably because bile was reabsorbed from the ducts. A pt. given a series of gold treatments for arthritis (total about 1.8 g metallic gold) died of carcinoma of the liver, with cirrhosis; gold content of the cirrhotic liver was 200 µg/g (3500 x normal) but the carcinoma contained no gold. Among 7 cases of arsenical cirrhosis, there were 2 deaths from bronchial carcinoma, 1 from lung carcinoma with metastases to liver; cirrhotic liver tissue contained 0.11 µg/g As, and 2 skin papillomas. The authors conclude that the role of heavy metals in the etiology of hepatic carcinoma requires further investigation.

64-685 A CLINICAL CONTRIBUTION TO THE STUDY OF BENZENE-INDUCED HEMOPATHIES AND PROBLEMS OF PREVENTION. (It.) De Dominicis, G. (Clin. Occup. Dis., Umberto I Hosp., Turin, Italy) and G. Buccini. Minerva Med. 54(92):3524-3529, 1963.

Detailed case histories are given for 4 pts. (3 female and 1 male, age 16-41 yr.) with various forms of pancytopenia (leukemic, hemocytoblastic or erythro-leukopenic). Diagnosis of acute hemocytoblastic leukemia was confirmed in 2 pts. Industrial exposure to benzene was proved in 3 pts. and suspected in the other. These findings confirm the possibility of the development of leukemia and related disorders of the hemopoietic system on the basis of long term benzene poisoning. Adequate protection of the industrial worker is stressed and preventive measures are discussed.

64-686 TWO-STAGE CARCINOGENESIS: EFFECT OF LENGTH OF PROMOTING TREATMENT ON THE YIELD OF BENIGN AND MALIGNANT TUMOURS. (E.) Roe, F. J. C. (Chester Beatty Res. Inst., London, S.W. 3) and J. Clack. Brit. J. Cancer 17(4):596-604, 1963.

Male and female strain S 12-week-old mice were painted with 1 application of 3,4-benzpyrene (BP; 300 µg in 0.2 ml acetone) which was followed after a 3-week interval by weekly applications of acetone (0.25 ml; Group I) or 0.1% croton oil (C0; 0.25 ml) for 10-77 wk. (Groups II-VII); controls received acetone initially and then 35 or 77 weekly applications of C0, resp. The cumulative total (in percent) of mice with a benign skin papilloma of 1 mm or more in diameter for 2 or more wk., the incidence of papillomas/survivor 2 wk. after the end of C0 treatment, and the cumulative total of malignant skin and probably malignant tumors at 90 wk. in the following groups were: Group II (10 wk. of C0), 2.5%, 0.05, and 3; Group III (20 wk. of C0), 50%, 1.22 and 4; Group IV (30 wk.), 44%, 1.22 and 1; Group V (40 wk.), 72%, 5.25 and 8; Group VI (50 wk.), 87%, 6.54 and 15; Group VII (77 wk.), 90%, not stated, and 16, resp. These results indicate that the prolongation of promoting treatment increased the incidence of malignant tumors. In Group I, 7 mice had skin papillomas, but at no time did the incidence exceed an av. of 0.15 papillomas/survivor; no malignant skin tumors occurred in this group. In the group treated with 35 wk. of C0 but no BP, 26 mice developed papillomas with an incidence of 1.67/survivor; 3 malignant skin tumors also occurred. The other group treated for 77 wk. with C0 but without BP had an av. incidence of 4.57 papillomas/survivor and 1 malignant tumor was seen. The incidence of malignant tumors other than those of the skin showed no obvious relation to treatment. All groups showed malignant lymphomas including reticulum cell sarcomas, myeloid leukemia (except in Groups II and III),

and local lymph node and distant metastases from malignant skin tumors (except Groups I and II). Other tumors such as eosinophilic leukemia, cavernous hemangioma, undifferentiated abdominal tumor, and adenocarcinoma of the lung, ovary, mammary gland or salivary gland occurred. (See also CRA 1(8):#1531, 1963 and the following abstract.)

- 64-687 AN ACTUARIAL METHOD OF ANALYSIS OF AN EXPERIMENT IN TWO-STAGE CARCINOGENESIS. (E.) Pike, M. C. (University Coll. Hosp. Sch. Med., Gower St., London, W.C.1.) and F. J. C. Roe. Brit. J. Cancer 17(4):605-610, 1963.

A standard actuarial method for analyzing age-specific death rates from a particular cause was described for the results of experiments outlined in the preceding abstract with reference to the papilloma data. An interrelation was seen between the effects of the initiating treatment with benzpyrene (BP) and the effect of the length of promoting treatment with croton oil (CO). Female mice developed papillomas more consistently than males, and for both sexes the difference in the rate of induction of first papillomas between mice continuing to receive CO and for mice in which treatment ceased, became evident within a few wk. after the change in treatment. Mice receiving CO treatment without BP-pretreatment developed their first papillomas consistently later than mice receiving CO treatment after initiating treatment with BP, although continued CO treatment alone induced at least 1 papilloma in almost all the mice.

- 64-688 PROGRESS REPORT: TUMOR DEVELOPMENT FOLLOWING INJECTION OF CARCINOGENS AT MULTIPLE SITES. (E.) Brues, A. M., H. Auerbach and G. DeRoche. Pp. 49-56 in Argonne National Laboratory. Biol. Med. Res. Div., Semiannual Report, July-Dec., 1962. ANL-6790. Biol. Med. (TID-4500, 27th Ed.), U. Chicago, Ill. Contr. W-31-109-eng.-38. Off. Tech. Ser., Dept. Comm., Washington, D. C., 236 pp., \$3.00, 1963.

Female Sprague-Dawley rats were given 1, 2 or 8 inj. of 20-methylcholanthrene (MC; 0.25 mg of a 0.5% soln. in trioctanoin s.c.) into the flank (in different sites of the flanks in the case of multiple inj.), while female Wistar rats received 8 inj. of MC; controls were given 0.05 ml of the solvent. About 45% of the controls and 60% of the MC-treated animals developed benign mammary tumors in over 500 days; therefore, MC had no effect on the time of development of the benign mammary tumors that are common in these animals. The incidence of malignant tumors (usually sarcomas) induced by MC, the av. latent period and the av. time to death after tumor appearance after the various inj. were: 1 and 2 inj., 61.9% and 60.7%, resp., 255 days and about 80 days; Sprague-Dawley and Wistar rats given 8 inj., 91.7% and 85%, resp., about 170 days and 80 days.

The mean doubling time in vol. of the malignant tumors in the various groups ranged from 6-10 days and that of the benign tumors in all groups was approx. 40 days. The av. time to first appearance of malignant tumors and to subsequent death was so much shorter than that for the benign mammary tumors that very little overlap in the 2 types of tumors occurred and thus, very few of the animals with malignant tumor ever developed a mammary tumor, although MC-treated rats not developing malignant tumors developed the normal control incidence of mammary tumors. The incidence of multiple malignant tumors varied from 4.8% in the 1-inj. group to 7.1% in the 2-inj. group, 45.8% in the 8-inj. Sprague-Dawley group and 45% in the 8-inj. Wistar group; the difference between the 2-inj. group and the combined 8-inj. groups was statistically significant. All the animals, except 1 in the 8-inj. group with 4 malignant tumors, showed 2 or 3 tumors.

- 64-689 THE PHASE OF THE HAIR CYCLE AT THE TIME OF CHEMICAL CARCINOGEN EXPOSURE AND EPIDERMAL TUMOR DEVELOPMENT IN MICE. (E.) Weidenreich-Sherwin, R. (Dept. Derm., New York U. Sch. Med., N. Y.) and F. Herrmann. Dermatologia (Basel) 128(3):232-238, 1964.

After inj. of the skin with 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.5% soln. in benzene, 0.05 ml) of Swiss albino mice, a higher tumor incidence was found when the DMBA was applied during the telogen, or resting phase, of the hair cycle (54% in females; 44% in males) than during the anagen, or growing phase (37% in females; 29% in males). Females showed a higher incidence (24/78) of tumor-bearing mice when DMBA application took place during the early stages (I-IV) of the anagen phase. It is recommended that the influence of the sex of the animal and the stage of the hair cycle on the tumor yield as a result of the action of carcinogenic or anticarcinogenic agents be considered in any study of such agents.

- 64-690 INTERACTION OF NUCLEIC ACIDS. II. CHEMICAL LINKAGE OF THE CARCINOGEN 3,4-BENZOPYRENE TO DNA INDUCED BY PHOTORADIATION. (E.) Ts'o, P. O. P. (Johns Hopkins U., Baltimore, Md.) and P. Lu. Proc. Nat. Acad. Sci. USA 51(2): 272-280, 1964.

In studies on the physical binding of tritiated 3,4-benzpyrene (BP), or its degradation products, with highly polymerized calf thymus DNA, photoradiation at the absorption band of BP for 4 hr. resulted in a "yield" of 53% of the covalent-linked photoproduct (DNA-BP). Radiation wavelengths above 340 mμ were shown to be responsible for the DNA-BP formation. Results of further studies by precipitation and extraction, sedimentation, electrophoresis, spectroscopy, enzymic hydrolysis and paper chromatography of the hydrolyzed products confirm these findings.

-691 ON THE REPORTED SOLUBILIZATION OF CARCINOGENIC HYDROCARBONS IN AQUEOUS SOLUTIONS OF DNA. (E.) Giovannella, B. C. (Ardle Mem. Lab., U. Wisconsin, Madison), E. McKinney and C. Heidelberger. *J. Molec. Biol.* 8(1):20-27, 1964.

A refutation of previously published data by Lyland and Green as well as Liquori et al., the authors have shown that when a 0.05% soln. of DNA in distilled water is ground with 3,4-benzene or 1,2,5,6-dibenzanthracene (both 5 mg) and the aqueous colloidal suspension of the formed hydrocarbon is sedimented completely with high speed centrifugation or filtered completely by a Millipore filter of uniform pore size, the only role DNA plays in this phenomenon is stabilization of the colloid to some extent; this effect was also duplicated with the use of soap instead of DNA. This evidence disproves a non-enzymic interaction of carcinogenic hydrocarbons with DNA and the interpretation of intercalation.

692 QUANTUM-CHEMICAL STUDIES OF CHEMICAL CANCEROGENS. (E.) Zahradnik, R. (Inst. Phys. Chem., Czech. Acad. Sci., Prague). *Plasma (Bratisl.)* 10(6):581-584, 1964.

A correlation found between carcinogenic activity of organic substances and their quantum-chemical properties indicates that a chemical reaction is the efficiency-determining factor. This structure-activity relationship has proved to be a criterion for the estimation of the carcinogenic activity of many derivatives, benzenoid hydrocarbons and derivatives of pyrrole and azo-compounds. The authors caution that, if a physical process is the efficiency-determining factor, these chemical properties become invalid for estimation of carcinogenic properties.

693 CHANGES IN THE SUBCUTANEOUS CONNECTIVE TISSUE OF THE RABBIT EAR IN THE PROCESS OF TUMOR DEVELOPMENT INDUCED BY 9,10-DIMETHYLBENZANTHRACENE. (E.) Ou, Pao-Hsiung. (Inst. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). *Bull. Exp. Biol. Med.* 55(2):191-193, 1964.

Translation from the Russian of a paper abstracted as CRA 1(2):#215, 1963.

694 SOME BIOLOGICAL ASPECTS OF SKIN CARCINOGENESIS. (E.) Boutwell, R. K. (Ardle Mem. Lab. Cancer Res., Madison, Wisc.). *Exp. Tumor Res.* 4:207-250, 1964.

A review and discussion on skin carcinogenesis (references), selective breeding of Rockland-derived mice showed that only 30% of the original S-1 generation mice developed tumors (papillomas) after a single application of 9,10-dimethyl-1,2-benzanthracene (DMBA; 75 µg in 25 µl benzene) followed 1 wk. later by semiweekly

applications of croton oil (CO; 125 µg in 25 µl benzene for 18 wk. for first 2 generations, 12 wk. thereafter), whereas 100% of the S-7 and following generations developed tumors 12 wk. after DMBA. After selection for resistance for 5 generations, tumor incidence was less than 20% at 12 wk. When increasing amounts of DMBA (0.5-50 µg) followed by CO (0.5%) were given, the tumor response increased rapidly from 0.9 papillomas/mouse at 0.5 µg of DMBA to an av. of 8.0 tumors/mouse at 10 µg, but the tumor response was not enhanced proportionately by 50 µg of DMBA. Mice obtained from other sources (such as Cumberland ICR, Carworth CF1, etc.) were not as responsive to papilloma or malignant skin tumor formation as the bred susceptible mice. In various experiments on initiation and promotion, there was no decrease in tumor response in mice treated with DMBA, followed 16 wk. later with CO as compared to groups in which there was no interruption between the initiator and the promoter; the promoting effect of CO was cumulative only if given in a sufficient amount at each application and if the interval between application was not too long. There was a threshold for the amount of CO that must be used in each application in order to achieve promotion. Also noted was the inability of exogenous factors to alter initiation, while the promotion process was inhibited dramatically by the imposition of caloric restriction or cortisone treatment. Various other experiments showed that tumor induction was a 3-step process.

64-695 THE DISTRIBUTION OF COPPER IN THE TISSUES OF THE RAT: THE EFFECTS OF AGE AND OF FEEDING p-DIMETHYLAMINOAZOBENZENE WITH AND WITHOUT COPPER ACETATE. (E.) Fare, G. (Dept. Path., U. Birmingham Sch. Med., England) and D. L. Woodhouse. *Brit. J. Cancer* 17(4):775-786, 1963.

Female 4-5-month-old rats were fed a maize (M) diet (Group I), M + dimethylaminoazobenzene (DAB; 0.09%; Group II) or M + DAB (as above) + copper acetate (CuAc; 0.05%; Group III) 5 days/wk. The DAB-fed rats had dark, roughened livers with scattered black nodules when examined after 156 and 193 days, followed by more pronounced liver changes; cystic and solid liver tumors were seen in several of the animals. The addition of CuAc to DAB delayed these changes and provided good protection against tumor formation; 1 of these rats on day 504 had a normal liver. The nitrogen content of liver homogenates (in mg Kjeldahl nitrogen/100 mg of filtered liver pulp) in Group II decreased to 2.04 as compared to the value of 3.41 for Group I after 290 days; in Group III, the nitrogen content was 2.80 after 504 days. In Group I, the copper content of the spleen, kidney and liver, in this order, increased slowly with time, while in Group II, there was a rise in the copper content of the liver and a decrease in that of the kidney, but the splenic level remained constant; the total amount of copper in the 3 organs, of the latter group expressed in terms of nitrogen, was identical with that of the control Group I. In Group III, the liver copper content/mg nitrogen

after 500 days increased 45x, the kidney content 2.3x and that of the spleen by 1.4x the normal value. (See also CRA 1(12):#2112, 1964.)

- 64-696 EXPERIMENTAL SUBMAXILLARY GLAND TUMORS IN RATS. HISTOLOGY AND HISTOCHEMISTRY. (E.) Cataldo, E. (Dept. Oral Path., Tufts U. Sch. Dent. Med., Medford, Mass.), G. Shklar and H. H. Chauncey. Arch Path. (Chicago) 77(3): 305-316, 1964.

Pellets of powdered 9,10-dimethyl-1,2-benzanthracene (5 mg) were implanted in the submaxillary glands of 36 albino rats (18 male, 18 female; age 3-4 mo.). The relatively constant sequence of changes consisted in degenerative, proliferative, metaplastic and malignant neoplastic phases. The neoplasms were epidermoid and adenocarcinomas and a fibrosarcoma. There was a decrease in succinic dehydrogenase and nonspecific esterase activity in the transition from normal to neoplastic tissue. The activity of acid phosphatase and β -D-galactosidase was not appreciably altered.

- 64-697 PRODUCTION OF MAMMARY TUMOURS WITH 3-METHYLCHOLANTHRENE. (E.) Daniel, P. M. (Maudsley Hosp., Denmark Hill, London, S.E.5) and M. M. L. Prichard. Nature (London) 201:578-580, 1964.

Young female Sprague-Dawley rats were admin. 20-methylcholanthrene (MC; 10 mg 3x/wk. x 7 by stomach tube; dissolved in sesame or olive oil) at various ages (Group I, age 42-49 days; Group II, age 61-66 days; Group III, age 79 days). In Group I, 10/12 (83%) developed 7 mammary adenomas and 3 fibroadenomas 4-57 wk. after the end of MC, while in Group II, 6/10 (60%) developed 5 mammary adenomas and 1 fibroadenoma 8-26 wk. after the end of MC; of Group III, 8/13 (61%) developed 6 mammary adenomas and 2 fibroadenomas 12-44 wk. after the end of MC. A few rats (number not stated) developed fibroadenomas in addition to their adenomas, and 1 rat developed an adenoma, a fibroadenoma and an anaplastic tumor along the milk-line. (See also CRA 2(3):#488, 1964.)

- 64-698 INDUCTION OF CANCER IN RATS BY SINGLE DOSES OF METHYLNITROSOUREA AND OF VARIOUS DIALKYLNITROSAMINES. (Ger.) Druckrey, H. (Dept. Surg., U. Freiburg i. Br., Berlin, Germany), D. Steinhoff, R. Preussmann and S. Ivankovic. Zschr. Krebsforsch. 66(1):1-10, 1964.

For earlier work on nitrosamines and nitroso compounds, see CRA 1(2):#217; *ibid.*, (7):#1264, 1963; and *ibid.*, (12):#2107, 1964. Single doses of 6 nitrosamine derivatives (dimethyl, diethyl, methylvinyl, ethylethanol, and ethylbutyl nitrosamine as well as nitrosomorpholine), given p.o., i.v., or by inhalation, produced a wide variety

of malignant tumors in 15 rats within 270-695 days. Malignancies of the kidneys were predominant, but carcinomas of the liver, esophagus, ovaries and nasal sinuses were also obtained. N-methyl-N-nitrosourea, 70-100 mg/kg i.v. in a single dose, was given to 16 BD rats. All died after 320 ± 40 days: 13 developed carcinomas (tongue 1, jaw 2, stomach 4, intestine 5 and breast 1); among 11 sarcomas there were 7 of the kidney. Four had benign papillomas and hyperkeratoses of the stomach. These findings are interpreted as evidence that carcinogenesis is an "accelerated process", which, once initiated by a single impulse, will continue to progress irreversibly.

- 64-699 SYNERGISM AMONG ORAL CARCINOGENS AND TUMORIGENS. REPORT OF PRELIMINARY EXPERIMENTS. (E., Abstract) Deichmann, W. B. (Dept. Pharmacol., U. Miami Sch. Med., Coral Gables, Fla.) and J. L. Radomski. Toxic. Appl. Pharmacol. 6(3):343-344, 1964.

Two preliminary experiments were carried out to determine if bladder carcinogens may be synergistic in the dog and whether 4 liver tumorigens are synergistic in the rat. Of 5 female beagle dogs fed 2-aminonaphthalene (0.1 g 5x/wk. for 31 mo. max.), 1/5 developed severe bladder cancer and 3/5 had a few small malignant tumors. No bladder cancer developed in 5 dogs fed 4-nitrophenyl (0.1 g 5x/wk. for 31 mo. max.). Severe bladder cancer developed in 5/5 dogs fed a combination of both compounds (same dosage as above). After 2 yr. of feeding with a mixture of 2-(p-tert-butylphenoxy)isopropyl-2-chloroethyl sulfite (Aramite), 1,1,1-trichloro-2,2-bis(p-methoxyphenyl)ethane (Methoxychlor), 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane (DDT), and thiourea at a level of 50 ppm for each compound, Osborne-Mendel male rats (not females) showed a higher incidence of liver cancer than did controls.

- 64-700 STUDIES OF NICKEL CARCINOGENESIS: FRACTIONATION OF NICKEL IN THE ULTRACENTRIFUGAL SUPERNATANT OF LUNG AND LIVER BY DEXTRAN GEL CHROMATOGRAPHY. (E., Abstract) Sunderman, F. W., Jr. (Dept. Med., Jefferson Coll. Med., Philadelphia, Pa). Am. J. Med. Sci. 247(5):633-634, 1964.

Normal rat lung homogenates were subjected to 105,000 x g centrifugation; after dextran gel chromatography, the supernatants contained 2 fractions: 72% of the nickel was present in the more rapidly migrating fraction, and was associated with macromolecular components, including RNA and proteins; 28% was in the slowly migrating fraction. Following acute and chronic exposure of rats to nickel carbonyl inhalation, increases were noted in both fractions. In the liver of exposed rats, there were increases in 2 macromolecular fractions, with little change in a slowly moving fraction.

701 REACTION OF THE CARCINOGEN DIMETHYL-NITROSAMINE WITH LIVER THIOL GROUPS *VIVO*. (E., Abstract) Craddock, V. M. (Microcol. Res. Unit, Carshalton, Surrey, England). *Chem. J.* 90(2):33P, 1964.

S were given dimethylnitrosamine- C^{14} (30 mg and $\mu C/kg$ i.p.) and sacrificed 5 hr. afterwards. acid soluble fraction of the liver was hydrolyzed, obtaining S-methyl-L-cysteine from any methylated precursors present. Carrier S-methyl-L-cysteine was added and the preparation chromatographed. The S-methylcysteine region was further analyzed by column chromatography. In one case, this product retained its radioactivity, indicating that dimethylnitrosamine, by its ability to methylate, can lead to the formation of a small amount of S-methylcysteine in the liver.

702 SKIN CARCINOMA IN THE PROCESS OF "STANFORD JOINTING". (E.) Spink, M. S. (Gen. Infirmary, Blackburn, England), A. H. Baynes and J. B. L. Tomblinson. *Brit. J. Industr. Med.* 21:154-157, 1964.

Two cases of squamous cell carcinoma resulting from exposure to mineral oil in the process of treatment of pipes known as "Stanford jointing" are described, being the first to be noted in this country. Two men, age 50 and 56 yr., who had "Stanford jointers" for 35 and 17 yr., resp.,

developed squamous cell carcinoma of the scrotum, while a third man, age 61, who had been a "Stanford jointer" for 17 yr., developed squamous cell carcinoma on the anterior aspect of the right forearm. The process itself is described with illustrations, and attention is drawn to the importance of realizing that such cases may occur in industrial processes where there is considerable exposure to mineral oil.

64-703 IMMUNOLOGICAL RESPONSE DURING CHEMICAL CARCINOGENESIS. I. NON-SPECIFIC ANTIBODY PRODUCTION. (E.) Lin, F.-J. (Dept. Biochem., Natl. Taiwan U. Coll. Med., Taipei) and T.-C. Tung. *J. Formosa Med. Assn.* 62(4): 344-348, 1963.

Male Long-Evans rats were fed a B₂-deficient diet 1 mo. before and 30 wk. after the addition of 0.06% dimethylaminoazobenzene (DAB). Both controls and DAB-fed rats were immunized (i.p.) at different periods with RBC of the mouse (NIH). Hemagglutination reactions of the RBC by the rat sera revealed a parallel rise and fall in antibody titers for all DAB-fed and control groups. In a comparison of primary and secondary responses after immunization, DAB-fed groups not only showed no lowering of antibody response, but seemed to have slightly higher antibody titers than did control groups. Thus, carcinogenesis did not mean an impairment in the production of circulating antibodies.

See also abstract nos.: 605,606,608,609,
618,622,641,706

VIRAL CARCINOGENESIS

- 64-704 VIRUSES IN CULTURES OF HUMAN LEUKEMIA CELLS. (E.) Stewart, S. H. (NCI, Bethesda), E. Lovelace, J. Landon and J. McBride. *Lavori Ist. Anat. Univ. Perugia* 23(3):153-166, 1963.

Cultures of bone marrow cells and peripheral blood leukocytes taken from pts. with leukemia developed monolayers which later became fibroblastic. The fibroblastic cultures usually formed small foci of piled up round cells with dark granular forms, which were maintained indefinitely and which showed no cytopathogenic changes. Non-fibroblastic cell cultures showed no evidence of mitosis but did show active metabolism as demonstrated by the pH change of the culture fluid. Electron microscopy showed the existence of similar virus-like particles in 3-4-wk. leukocyte cultures obtained from 4 different pts. BALB/c mice and Syrian hamsters were thymectomized 12-24 hr. after birth and inoc. by s.c., i.p., intracerebral or intrathoracic routes with culture fluid. In a 13-16-mo. observation period, although only 2 mice developed tumors (mammary adenocarcinomas), thymectomy was not tolerated well and many developed runt disease, pneumonia and hepatitis. A high incidence of lymphomas was seen in both inoc. hamsters and in controls (thymectomy only), while proliferative lung lesions were observed in 20 inoc. hamsters and in 2 controls. The particles described morphologically resemble the murine leukemia viruses and some particles found in human leukemias, but have not as yet been demonstrated as the cause of the proliferative lung lesions.

- 64-705 CONCENTRATION AND CHROMATOGRAPHY OF THE INFECTIOUS AND HEMAGGLUTININATING ACTIVITY OF POLYOMA VIRUS. (Fr.) Daniel, P. (Pasteur Inst., Paris) and J.-L. Delsal. *Path. Biol. (Paris)* 12(1-2):43-46, 1964.

CES polyoma virus grown on embryonal mouse cells was precipitated at room temperature with ammonium sulfate (pH 7), with 15% ethyl alcohol (4°C, pH 4), or with 50% ethyl alcohol (pH 7). Purification of the conc. viral suspension on DEAE-cellulose column and testing of successive fractions on mouse embryo cells showed a very close correlation between hemagglutinating activity (HA) and cytopathic effect. RS polyoma virus suspensions grown on monkey kidney cells and conc. by precipitation with 15% ethyl alcohol, as above, lacked HA even at conc. of 100x; after chromatography on DEAE-cellulose column, cytopathic activity was demonstrable only after the 3rd and subsequent passages on mouse embryo cells.

- 64-706 VIRUS TUMOR PROBLEMS. FIRST CONFERENCE OF THE EUROPEAN VIRUS TUMOR GROUP IN LONDON (SEPTEMBER 2-4, 1963). (Dut.) Links, J. *Nederl. T. Geneesk.* 108(14):719-721, 1964.

C. G. Ahlström reported that Rous Sarcoma virus (RSV) showed a significant increase of carcinogenic activity in newborn, inbred rats treated with cortisone or cortisol if the passage immediately preceding was made through a chicken, but not through a duck; passage of the duck-RSV through a hen makes it then increase rapidly when inj. into young rats, possibly because RSV forms an extra viral covering out of cell-wall material (proteins + phospholipids and other lipids) in the course of tumor formation. N. G. E. Jonsson reported that RSV tumors in mice, transplanted from hens, were formed from the cells of the host, not from those of the donor chicken. L. N. Payne and P. M. Biggs reported that embryos of 2 substrains of White Leghorn chicken (C and I) showed markedly different degrees of genetically-determined resistance to RSV. B. Lagerlöf reported evidence suggesting that the virus causing myeloid leukemia in chickens can induce tumors of the internal organs and/or anemia, instead of leukemia, in certain strains or in the presence of certain levels of immunologic or infectious tolerance. O. Berenblum then suggested that a population of related viruses might be involved in this phenomenon; Virus A becoming active in 1 host, Virus B in another. L. Fiori said that placing newborn BALB/c mice with an RIII foster mother resulted in a significantly higher percentage of spontaneously occurring leukemias at maturity (RIII being an inbred strain in which relatively many spontaneous mammary tumors arise in adulthood). J. F. Duplan reported demonstrating a leukemia virus in C57/BL mice in which leukemia had been induced by X-irradiation. M. H. Salaman, B. W. J. Mahy and K. E. K. Rowson discussed the Riley virus at length, a virus which is not as yet associated with any disease but which raises serum lactate dehydrogenase and phosphohexoisomerase activity in mice exactly like the leukemia-inducing Moloney virus. M. G. P. Stoker found that a cell line of hamster fibroblasts relatively resistant to X-rays was more quickly transformed into tumor cells by polyoma virus than a non-resistant strain. According to Y. Berwald, this polyoma-virus infected strain of hamster fibroblasts is resistant to the action of the carcinogens 3,4-benzpyrene and 4-methylcholanthrene. Stoker, however, suggests that this resistance may be due to selection of cells with certain properties rather than a change in properties due to the virus. G. J. Barski reported that chick embryos infected with the virus of herpes simplex and then with polyoma virus produced only the latter, but without tumor formation, indicating that the former acts as a tumor-inhibitor in this combination. (See also CRA 1(6):#1147, 1963.)

- 64-707 STUDIES ON AMINO ACID INCORPORATION INTO PROTEIN OF TUMORS INDUCED BY ROUS SARCOMA VIRUS AND HYPERPLASIA INDUCED BY FOWL POX VIRUS IN CHORIOALLANTOIC MEMBRANE OF CHICKEN EMBRYOS. (E.) Wagle, S. R. (Dept. Pharmacol., Indiana U. Sch. Med., Indianapolis), J. Ashmore

and A. S. Levine. Cancer Res. 23(11):1808-1812, 1963.

Comparisons were made of the rate of incorporation of C^{14} -labeled L-amino acids into protein of chicken embryo chorioallantoic membrane (CAM) of 10-day-old chicks infected with Rous sarcoma virus (RSV) and a nontumor virus (fowl pox virus; FPV). In *ovo* studies of glycine- C^{14} (1 mg = 1 μ C of C^{14} /0.2 ml of RSV) incorporation into the protein of RSV-induced tumors showed a progressive increase in protein specific activity from days 3-6 following infection of the CAM. Cell-free homogenate fraction comparisons showed the pH-5 enzyme-microsome system of Rous tumors to have a 3-4 fold increase in amino acid incorporation into protein over that observed with similar preparations from CAM or FPV-infected tissues. When combined with rat liver microsomes, Rous tumor pH-5 enzymes were ineffective, but alone they increased the amino acid incorporation activity of CAM and chick embryo liver microsomes. In *vitro* incubation of tissue slices with C^{14} -labeled glycine, glutamate, and leucine showed a 1-2 fold increase in amino acid incorporation into protein of Rous tumors and fowl pox hyperplasia when compared with uninfected (control) CAM from embryos of the same age.

64-708 THE FATE OF PARENTAL PRELEUKEMIC CELLS IN LEUKEMIA-SUSCEPTIBLE AND LEUKEMIA-RESISTANT F₁ HYBRID MICE. (E.) Metcalf, D. (Walter and Eliza Hall Inst., Royal Melbourne Hosp. Post Office, Victoria, Australia). Cancer Res. 23(11):1774-1781, 1963.

A high incidence of spontaneous lymphoid leukemia (89%) was found to develop in (AKR x C3H)F₁ mice, whereas in (AKR x C57BL)F₁ hybrids it was only 8%, with an increasing incidence (>16%) of reticulum cell sarcomas. Pooled 6-month-old preleukemic AKR spleen cells were inj. i.p. into 2-5-day-old mice of both groups. In the (AKR x C57BL)F₁ recipients, reticular tumors of AKR type appeared 40 wk. later than those in normal mice, but about two-thirds were reticulum cell sarcomas rather than lymphoid leukemias; the (AKR x C3H)F₁ hybrids behaved as the AKR donors. (See also CRA 2(2):#310, 1964.)

64-709 STUDIES ON THE TRANSMISSIBILITY AND CYTOLOGY OF THE RENAL CARCINOMA OF RANA PIPPIENS. (E.) Roberts, M. E. (Dept. Pathobiol., Johns Hopkins U., Baltimore, Md.). Cancer Res. 23(11):1709-1714, 1963.

When frogs were inj. i.p. with 0.5 ml of a tumorous kidney inoculum and a control group was inj. i.p. with 0.5 ml of a normal kidney inoculum, there was no significant difference in total tumor incidence and there was no difference as regards sex. Histological examination revealed that 54/61 tumors were of Type I and were obtained from frogs kept at 20-25°C; 7/61 were Type II

obtained from frogs kept at 5°C without being fed for at least 2 mo. Type I tumors had enlarged cells and all tumors showed mitotic activity; Type II tumor cells appeared to be necrotic or degenerating and mitotic activity was rarely seen.

64-710 CONGENITAL ANOMALIES AND VIRUS INFECTIONS. (E.) Evans, T. N. (Dept. Obstet. Gynec., U. Michigan, Ann Arbor) and G. C. Brown. Trans. Am. Gynec. Soc. 86:191-203, 1963.

Antibody titers for all of the Coxsackie B group viruses, Type A-9 of Coxsackie A viruses, E-6 and E-9 in the Echo group viruses, and influenza A and B virus were measured from blood samples taken at initial examination and at delivery of 4000 pregnant women to determine if these viruses had teratogenic properties. The incidence of significant changes in the antibody titers for those with birth anomalies and the controls was: for Coxsackie A-9, 6:1; for Coxsackie B-2, 5:2; for Coxsackie B-4, 7:2; and Echo 9, 4:1. Considered as a group, these 4 viruses appear to be related to the incidence of congenital malformations. In 137 pts. with anomalous infants, stillbirths or abortions, incidence of adenovirus, Echo 9 and Coxsackie B-4 antibodies was 37, 44 and 91, resp., as compared to 25, 39 and 80, resp., in matched controls. Neither stillbirth nor abortion could be associated with a particular virus.

64-711 CULTURE OF THE MOUSE MYELOID LEUKEMIA VIRUS ON HOMOLOGOUS TISSUE CULTURE SUBSTRATES. (Ger.) Graffi, A. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin, Berlin-Buch) and T. Schramm. Acta Biol. Med. German. 11(5/6): 929-933, 1963.

Resuspended sediments (0.1-0.3 ml) of the culture medium of mouse embryo cells (originally inoc. with cell-free preparations from various leukemic mouse tissues) were inj. s.c. into newborn mouse strains (CBA, XVII, C57BL and Agnes Blum): leukemia developed in 62/143 (44%) of those inj. with material from the original culture and in 19/54 (26%) with material from subsequent passages (in some cases as high as 90%). Occasionally mice were inoc. also with cell-containing material, or with material obtained from culture passages. Among 110 control mice inj. with sterile culture medium or organ extracts from healthy mice, only 1 case of leukemia appeared. Among the 62 inj. with material from the primary cultures the following leukemia types appeared: 24 myeloid, 10 paramyeloid, 2 myeloid-reticular, 5 reticular-myeloid, 3 reticulum cell, and 18 unspecified; 1 lymphatic leukemia occurred. It was noted that culture material from mice with reticulum cell leukemia also produced myeloid leukemias. The leukemogenic activity of the cultures fluctuated, but remained essentially around the same levels over the 61 days (max.) culturing period (approx. 14 changes of media or passages). This activity was manifest in both cell-free material and culture cells, the

latter having a high conc. of virus. (See also CRA 1(5):#943, 1963; and *ibid.*, 2(4):#712, 1964.)

64-712 CULTURE OF THE MOUSE MYELOID LEUKEMIA VIRUS ON HETEROLOGOUS TISSUE CULTURE SUBSTRATES. (Ger.) Schramm, T. (Inst. Exptl. Cancer Res., German Acad. Sci., Berlin, Berlin-Buch) and A. Graffi. *Acta Biol. Med. German.* 11(5/6):934-936, 1963.

Cell-free extracts (see preceding abstract) of leukemic mouse lymph nodes were inoc. into various tissue and cell cultures; highspeed centrifuged culture extracts were then inoc. into newborn CBA, XVII, C57BL, and Agnes Bluhm mice. After use of rat embryo material, leukemia developed in 17/47: 5 myeloid (including 2 chloroleukemia), 1 paramyeloid, 3 myeloid-reticular, 2 reticular-myeloid, 2 reticular, 4 unclassified; av. latent period was 204 days. Material from a passage of this rat embryo culture caused leukemia in 4/21 (233 days). HeLa cell culture material caused 11/16 leukemia: 5 myeloid (including 2 chloroleukemia), 1 paramyeloid, 2 myeloid-reticular, 1 reticular-myeloid, 2 unclassified; av. latent period 128 days. Material from a calf kidney culture caused 3/24 leukemia: 1 myeloid, 1 myeloid-reticular, 1 reticular-myeloid; av. latent period 240 days. Material from rat embryo + calf kidney culture caused 4/7 leukemia: 3 myeloid (including 2 chloroleukemia, 1 reticular-myeloid); av. latent period 160 days. The results with the HeLa cell culture indicate marked virulence; the leukemia types produced are similar to those produced by viruses from homologous cultures. (See also CRA 1(5):#943, 1963; and *ibid.*, 2(4):#711, 1964.)

64-713 RECENT STUDIES OF THE PROPERTIES OF MYELOID MOUSE LEUKEMIA VIRUS AND THE MEANS OF ACTIVATING IT. (Sp.) Graffi, A. (Inst. Exptl. Cancer Res., German Acad. Sci. Berlin, Berlin-Buch). *Sangre (Barc.)* 8(4):399-412, 1963.

A Spanish-language review (31 references) of some of the data presented in the two preceding abstracts (CRA 2(4):#711; and *ibid.*, #712, 1964) It is added that RNA isolated from the lymph glands of newborn mice bearing virus-induced leukemias induces leukemia in approx. 20% of newborn mice receiving it; RNase suppresses this action. DNA showed no leukemogenic activity. Immunization of adult, inbred XVIII, CR57, CRA or AkR mice with cells of an isologous myeloid leukemia induced resistance to reinoculation of the same leukemia in approx. 70% of the animals. The same new cellular antigen was demonstrable in all leukemic cells induced by the myeloid mouse leukemia virus employed, irrespective of the form of leukemia (myeloid, reticulo-cellular or lymphatic) developed, and shown by positive cross reactions between the various forms. The same antigen was also demonstrable, in the same way, in rat

leukemic cells produced by the virus, but no cross reaction occurred with leukemic cells from animals infected with Gross leukemia virus. The author concludes that the virus under study was different from the Gross strain. (See also CRA 1(5):#943, 1963.)

64-714 EFFECT OF X-IRRADIATION ON DNA SYNTHESIS IN POLYOMA VIRUS-INFECTED CULTURES. AUTORADIOGRAPHIC STUDIES. (E.) Minowada, J. (Roswell Park Mem. Inst., Buffalo, N. Y.). *Exp. Cell Res.* 33(1-2):161-175, 1964.

Autoradiographic studies, using H³-thymidine, to elucidate the changes of DNA synthesis in mouse-embryo cell cultures (in medium 199 + 10% calf serum + antibiotics) infected with polyoma virus (PV) Strain #2610-9 (10⁻¹⁵ x 10⁻⁴ HAU/cell allowed to adsorb for 3 hr. at 37°C) and immunofluorescent studies, to provide a measure of the presence of viral antigen in the infected cell, were carried out. Four sets of mouse embryo cultures were prepared: (1) non-irradiated cultures; (2) cultures X-irradiated at the time of seeding and 24 hr. before PV infection; direct X-irradiation of culture cells on cover slips 5 hr. after PV infection (3), or 24 hr. after PV infection (4). Although DNA synthesis as a result of PV infection can be ascribed to both host cellular and viral DNA, in X-irradiated PV-infected cultures the increase in DNA synthesis can be ascribed to newly synthesized viral DNA. Time curves of virus multiplication and of the increase in DNA synthesis were found to be similar in both X-irradiated and non-irradiated cultures infected with PV. X-irradiation of cell cultures at 5 or 24 hr. after PV infection showed the same pattern of DNA synthesis, virus multiplication and cytopathic effect as that observed in non-irradiated infected cultures, indicating the occurrence of a "radio-stabilization" effect in PV-infected cell cultures. It was suggested that host cellular DNA synthesis at the time of PV infection does not appear to be responsible for viral DNA synthesis. (See also CRA 1(1):#112; and *ibid.*, (2):#263, 1963.)

64-715 MOUSE LEUKAEMIAS. TYPING OF MOUSE LEUKAEMIAS BY SEROLOGICAL METHODS. (E.) Old, L. J. (Sloan-Kettering Inst. Cancer Res., New York), E. A. Boyse and E. Stockert. *Nature (London)* 201:777-779, 1964.

Antisera were prepared from various mice strains against leukemias induced by viruses (see CRA 1(7):#1353, 1963; and *ibid.*, 2(2):#205, 1964) and by other means. Cells of individual leukemias were examined for their sensitivity to these cytotoxic sera as well as for their capacity to absorb specific cytotoxic activity. It was found that against Friend, Moloney, Rauscher and TL (thymus leukemia) antisera the leukemias induced by Friend virus were +, +, +, -, resp.; those induced by Moloney virus were +, +, +, ±, resp.; those induced by Rauscher virus were +, +, +, ±, resp.; TL-induced

were -, -, -, +, resp.; those induced by Gross virus were -, -, -, ±, resp. No reaction occurred with AKR spontaneous and the chemically (percutaneous 9,10-dimethyl-1,2-benzanthracene)-induced leukemias.

64-716 SEX RATIO OF CHILDREN BORN OF LEUKEMIC MOTHERS. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda). *Pediatrics* 33(4):587-589, 1964.

In a review of world literature (10 references) from 1930-1963, studies on 73 offspring of 73 pregnancies associated with acute leukemia showed that there were 24 males and 32 females born alive and 9 males and 8 females born dead, sex ratio (male/female) = 0.83. Among 72 offspring of 68 pregnancies associated with chronic leukemia there were 37 males and 28 females born alive and 4 males and 3 females born dead, sex ratio (male/female) = 1.32. These differences were not statistically significant. No conclusive evidence of maternal-fetal transmission of leukemia was encountered.

64-717 PRODUCTION OF TYPE-SPECIFIC C ANTIGEN IN VIRUS-FREE HAMSTER TUMOR CELLS INDUCED BY ADENOVIRUS TYPE 12. (E.) Huebner, R. J. (NIH, Bethesda), H. G. Pereira, A. C. Allison, A. C. Hollinshead and H. C. Turner. *Proc. Nat. Acad. Sci. USA* 51(3):432-439, 1964.

After chromatographic fractionation of adenovirus Type 12 antigens, derived from infected 3T3 cells, into complement-fixing antigens A and B and testing their reaction with immune rabbit serum prepared from adenovirus 2, 12, 12-A and 12-C, it was found that A and C fractions were highly reactive with their homologous antisera, but nonreactive with heterologous sera. A serum pool from hamsters with primary tumors was found to react with C antigen, but not with A antigen. Individual serum antibody responses in hamsters carrying transplanted Type 2 tumors revealed partial correlation between antibodies to C antigen and antibodies to crude type 12 viral antigen, as well as correlation between C antigen and neutralizing antibodies. No evidence of antibodies to Type 12 C antigen was found in hamsters carrying tumors induced by adenovirus Type 18. Lack of A antigen was found in 80 individual sera from hamsters with Type 12 adenovirus-induced tumors. The reactions of A and C rabbit antisera were specific when tested with purified A and C antigens, but reactions with hamster tumor tissue antigens gave very low antigen titers (1:2-1:4) which appeared to some extent to be nonspecific and most likely due to Forssman immune response. (For earlier study, see CRA 1(9-10):#1740, 1964.)

64-718 STUDY OF A VIRUS ISOLATED FROM A CHLORO-LEUKEMIC WISTAR RAT. (E.) Lum, G. S. (VA Hosp., Cincinnati, Ohio) and A. W. Schreiner. *Cancer Res.* 23(11):1742-1747, 1963.

A nonpathogenic strain of rat virus, L-S strain, was isolated from one 43-day-old Wistar rat bearing chloroleukemia, while 5 other rats with chloroleukemia and 21 other tumor-bearing rats (Sprague-Dawley rats with chloroleukemic tumors and Wistar rats with methylcholanthrene-induced sarcoma, spontaneous sarcoma and X-ray-induced sarcoma in Wistar rats) yielded no virus. The L-S virus did not grow on embryonic mouse tissue but did grow on embryonic rat tissue and produced a cytopathogenic effect which was slightly different from that produced by Kilham's latent rat virus (RV). Various properties of the L-S virus are presented such as its stability under various storage conditions and after ether treatment as well as its serological relationship to RV. The distinctive characteristic of L-S strain is its lack of pathogenicity for hamsters.

64-719 SITES OF VIRUS PARTICLES IN CHIBA SARCOMA AS OBSERVED ON AN ELECTRON MICROSCOPE. (E.) Okano, H. (Cancer Res. Inst., Kyushu U. Sch. Med., Fukuoka, Japan), and T. Imai. *Kyushu J. Med. Sci.* 13(3):159-164, 1962.

Viruses found in intrathymic tumors obtained from 3 chicks killed 6-7 days after inoc. with Chiba chicken sarcoma were round or ovoid in shape, 70-85 mμ in diameter with a central nucleoid 30-40 mμ across. Some of the particles exhibited a double membrane. Most of the virus particles were found in the transitional area containing both Type A and Type B sarcoma cells, with greatest frequency and number in the former. The virus particles decreased in conc. toward the inner part of the aggregate and none were found at the center. The conspicuous sites of virus aggregation were the surface of the cell and the viroplast. The virus particles on the cell surface were situated at various intervals and close to the cell membrane, or were densely arranged in a single row there. The viroplasts contained either densely or loosely packed virus particles. Virus particles were found most frequently and most abundantly in the peripheral part of a focus of proliferation of the tumor cells.

64-720 ISOLATION OF VIRUSES FROM LEUKAEMIC PATIENTS. (E.) Negroni, G. (Div. Exptl. Biol. Virol., Imperial Cancer Res. Fund, London). *Brit. Med. J.* 1:927-929, 1964.

Bone marrow samples from 25 pts. with leukemia were inoc. into human embryo tissue cultures and viruses were successfully isolated and maintained by serial passage in 9 cases (4 female, 4 male, 1 sex not given; 4 acute leukemia, 1 acute lymphoblastic leukemia, 1 unspecified leukemia, 1 chronic myeloid leukemia, 1 Naegeli type leukemia). These viruses became cytopathic for the cells in the course of serial passage. Comparable cultures inoc. with bone marrow from 12 control cases (pts. with diseases other than leukemia) showed no changes even after many "blind" passages. The leukemic viruses, which are thermolabile and

ether-sensitive, at the time of report, produced no pathological changes after inoc. into newborn mice, hamsters, and ferrets. Three different virus isolates produced antibodies in rabbits and cross neutralization tests showed that all 9 strains of virus were antigenically related. Although results of neutralization tests with sera from leukemic pts. are still in a preliminary stage, sera from 8 leukemic (7 chronic lymphatic, 1 acute myeloid) pts., diluted in a 1:10 ratio, neutralized 10-100 TCID in 7/8 cases. Sera from 9 normal pts. with diseases other than leukemia showed no neutralization; two sera from pts. with "anemia" gave a doubtful result. (See also the following two abstracts.)

- 64-721 ELECTRON MICROSCOPY OF VIRUS PARTICLES IN CELL CULTURES INOCULATED WITH PASSAGE FLUID FROM HUMAN LEUKAEMIC BONE-MARROW. (E.) Inman, D. R. (Imperial Cancer Res. Fund, London, W.C.2), D. A. Woods and G. Negroni. *Brit. Med. J.* 1:929-931, 1964.

Electron microscope examination of 48-hour tissue cultures inoc. with passage fluid derived from human leukemic bone marrow showed the presence of virus particles in both the cytoplasm of the intact cells and in ultracentrifuged culture fluid pellets. The virus particles have an overall diameter (av_2) of 730 Å, an intermediate membrane of 500 Å, an electron-dense nucleoid of 420 Å and nuclear particles measuring 400 Å; neither cytoplasmic nor nuclear particles were seen in cultures 20 hr. after inoc. In negative contrast preparations the particles were 340 Å in diameter. The cytoplasmic particles are morphologically similar to, and in the same size range, as those seen in various mouse and avian leukemias and resemble virus-like particles found in association with cases of human leukemia as reported by others. (See also the preceding and following abstract.)

- 64-722 A LEUKEMIA VIRUS--PASSENGER OR DRIVER? (E.) Editorial *Brit. Med. J.* 1:921-922, 1964.

A discussion of the two previous papers and a review (17 references) considers two possibilities: the virus isolated from human leukemic marrow may be either the prime causative agent or a "passenger" which is not causally connected with the disease at all. Like the authors of the two papers referred to, this editorial stresses the fact that the isolated virus has not yet been shown to be causally related to leukemia.

- 64-723 UNIDENTIFIED, FILTRABLE AGENTS ISOLATED FROM AFRICAN CHILDREN WITH MALIGNANT LYMPHOMAS. (E.) Dalldorf, G. (Walker Lab., Sloan-Kettering Inst., Rye, New York) and F. Bergamini. *Proc. Nat. Acad. Sci. USA* 51(2): 263-265, 1964.

From 6/8 African children with malignant lymphomas (typical clinically and histologically) of the bones of the jaw, a number of cytopathogenic agents were recovered. Isolations made from bone marrow, tumor suspension supernate and feces of 4/6 patients failed to show recognized morphological changes when frequently passed into primary human amnion cell cultures (or Wistar cells), but fluids harvested from such cultures induced severe cytopathogenic changes preceded by marked nuclear abnormalities in either fetal lung (FL) or human embryonic kidney cell cultures. The isolated agents failed to induce disease in newborn mice or hamsters or immature monkeys of several species and though the sera from vervet monkeys inoc. i.m. with the agent had appreciable neutralizing antibodies, it failed to induce activity in complement fixation tests with adenovirus, influenza virus, and other viruses. Since the sera from healthy Kenya children inoc. with the isolated agents were frequently without activity, and the sera from leukemic patients inoc. with the agent had a neutralizing effect, it is hoped that serum surveys will help in determining whether these cytopathogenic agents are related to the disease.

- 64-724 CELL-FREE TRANSMISSION OF RADIOGENIC MYELOID LEUKEMIA IN THE MOUSE. (E.) Jenkins, V. K. (Oak Ridge Natl. Lab., Tenn.) and A. C. Upton. *Cancer Res.* 23(11):1748-1755, 1963.

Radiation-induced myeloid leukemia of the RF/Up male mouse was passaged in unirradiated newborn and adult RF recipients by i.v. inoc. of leukemic spleen cell suspensions, cell-free filtrates of such suspensions, and centrifuged (presumably cell-free) spleen extracts and blood plasma. The incidence of takes increased on successive passages, while the av. latency concurrently decreased. Although the leukemia retained its granulocytic and myelocytic character in adults, a significant number of newborn females developed thymic lymphomas (8% by 230 days, controls 1%); for males the 5% incidence was not significantly different from the controls but latency was greatly decreased. This suggested that the same agent can induce both types of leukemia, depending on the influence of host factors, or that more than one leukemogenic agent was present in the filtrates. Leukemogenic activity was not detected in filtrates of brain or spleen tissue from donors with primary radiogenic myeloid leukemia on inoc. into unirradiated recipients or those given 150-300 r of whole body X-rays, but such filtrates increased the incidence of myeloid leukemia in mice previously exposed to 450 r whole-body X-radiation, suggesting that radiation may enhance susceptibility to an otherwise undetectable agent. The short latency of the filtrate-induced leukemia (less than 6 wk.) contrasted sharply with the long latency of the radiation-induced leukemia (6-50 wk.) which may indicate that the leukemogenic action of radiation was not merely the "activation" or liberation of latent leukemia virus.

64-725 STRUCTURE OF VIRUS PARTICLES PARTIALLY PURIFIED FROM THE BLOOD OF LEUKEMIC MICE. (E.) De Harven, E. (Sloan-Kettering Inst. Cancer Res., New York) and C. Friend. Virology 23(1):119-124, 1964.

Adult mice (DBA/2) inoc. i.p. with the leukemia virus were bled from the axilla 2-3 wk. after inoc. when all the animals showed marked splenomegaly; the blood was chilled, pooled at 0° and mixed with an equal vol. of cold 0.15 M NaCl containing heparin (2 U/ml) and then was centrifuged; the resulting pellet (about 1 or 2 mm in diameter) was fixed with osmium tetroxide (OsO₄). Electron microscope studies of the pellets showed homogeneous spherical particles which, in shape and dimension, were indistinguishable from the virions observed in tissues of leukemic mice; particles were of both type A₁ and C and "tailed" forms were absent. After purification of another leukemic sample in 0.306 M potassium citrate, the virus pellets consisted of poorly preserved particles mixed with variable amounts of cellular debris and the outer envelope of the virion was poorly preserved and frequently formed "tails" of various lengths. After purification at the osmolarity of the plasma and combined positive (OsO₄) and negative staining (PTA), numerous round particles were seen which were identified with the virus; however, no tails were seen. After fixation in OsO₄ but purification in 0.306 M citrate before drying in PTA, all the particles showed the characteristic "tailed" forms. After purification in heparin-saline and drying in sodium phosphotungstate without prior fixation, most of the particles showed a "tailed" form, probably due to a hypertonic phase in the drying process.

64-726 ORAL TUMORS INDUCED BY POLYOMA VIRUS IN MICE. (E.) Stanley, H. R. (Natl. Inst. Dent. Res., Bethesda), C. J. Dawe and W. Law. Oral Surg. 17(4):547-558, 1964.

Polyoma virus (serially passaged on tissue cell culture line P388 D₁, a neoplastic cell line isolated from a transplanted malignant lymphoma of a DBA/2 mouse) was inj. s.c. into 11 mice (5 male, 6 female; Strains C3H/BiLw and C3H/BiLw x AKF/F₁). The following tumors were observed: gingival epithelium (dental) 47/70; nasal mucosa 8/70; lacrimal, oral submucous, and minor salivary glands 13/70; osseous tissue 2/70. The majority of the tumors arising from the gingival epithelium were of epithelial origin, occurred in the molar or incisal area, and presented several characteristics of human ameloblastoma. It is suggested that this type of tumor may represent a type of mouse ameloblastoma. The histopathology of the tumors is described.

64-727 STUDIES ON THE TUMORIGENIC PROPERTIES OF BABY HAMSTER KIDNEY CELL LINES AND METHOD OF SELECTION OF HIGH AND LOW TUMORIGENIC

CLONES. (E.) Gotlieb-Stematsky, T. (Dept. Microbiol., U. Tel Aviv, Israel) and R. Shilo. Virology 22(3):314-320, 1964.

When adult hamsters were inj. s.c. near the hind leg with established baby hamster kidney cell line BHK₂₁, tumors (fibrosarcomas with giant and spindle cells) developed in more than 50% of the animals upon inoc. of 10³ cells within 6-8 wk. and in 100% of the animals inoc. with 10⁴ cells within 3-4 wk., while inoc. of 10 or 100 cells did not produce tumors. Polyoma virus was not encountered when cells of various passages of baby hamster kidney cells (BHK₂₁, C₁₃, 1BH₃, 3BH₇) and cell lines were inoc. in mice. After hemagglutination inhibition tests and neutralization tests, no significant differences were found between test material and controls, nor were neutralizing antibodies found in any of the sera. In selecting tumorigenic cell clones from the "wild" BHK₂₁ cell line, better growth, 10-30% plating efficiency and increased tumorigenic properties were obtained with C₀₂ incub. Highly tumorigenic cell clones will produce tumors with as few as 10 cells, whereas the nontumorigenic clones will produce only an occasional tumor when 10⁵ to 10⁶ cells are inj. Cell arrangement in cell cultures was not correlated with the tumorigenic property.

64-728 AN ASSAY FOR CELLULAR TRANSFORMATION BY SV40. (E.) Todaro, G. J. (Dept. Path., New York U. Sch. Med., N. Y.) and H. Green. Virology 23(1):117-119, 1964.

A more detailed account of CRA 1(12):#2144, 1964. Cloning efficiency of line 3T3 varied from 30-50% and no decrease was seen even when cells were infected with the highest SV40 conc.; no detectable cytotoxic effects of SV40 were observed microscopically. Two wk. after plating, untransformed cells formed a confluent monolayer with no nuclear overlapping, while transformed colonies were multilayered. Infection with the most potent virus conc. (10^{8.4} TCID₅₀/ml) resulted in the production of transformed colonies from 0.75% of the cells plated; somewhat <2% of the cells infected were transformed. The ratio of transformed cells to infectious particles was 10⁻⁴-10⁻⁵ (a range similar to that reported for DNA-containing tumor viruses in other systems). Transformed 3T3 cells, once cloned, uniformly gave rise to transformed colonies. The authors feel that the system reported here should allow more precise analysis of factors involved in the transformation by SV40.

64-729 RESISTANCE OF BHK21 HAMSTER CELLS TO SV40 PAPOVAVIRUS. (E.) Rapp, F. (Dept. Virol., Baylor U. Coll. Med., Houston, Texas), K. S. Khera and J. L. Melnick. Nature (London) 201:1349-1350, 1964.

When hamsters were first immunized with SV40 virus and then challenged with 10⁴, 10³, and 10² SV40-treated BHK21 cells, tumors were seen in 6/6,

5/5 and 3/6 animals, resp.; with 10^4 , 10^3 , and 10^2 untreated BHK21 cells, tumors appeared in 6/6, 6/6, and 4/5 animals, resp. Similar results were obtained with control hamsters inoc. with SV40-treated BHK21 and untreated BHK21 cells. Control hamsters, as well as hamsters previously inoc. with SV40, developed tumors in cheek pouches after challenge with BHK21 cells. At the passages tested, the BHK21 cells were more tumorigenic than H-50 cells (derived from a virus-free hamster tumor induced by SV40). Marked resistance was noted in hamsters to the transplantation of H-50 cells after prior inoc. with SV40: after inoc. of 10^4 , 10^3 and 10^2 cells, there were, resp., 3/12, 1/10 and 0/10 tumors per pouch/pouches inoc. (See also CRA 1(12):#2142, 1964.)

- 64-730 DENSITY GRADIENT CENTRIFUGATION OF A MURINE LEUKEMIA VIRUS. (E.) O'Connor, T. E. (Lab. Viral Oncol., NCI, Bethesda), F. J. Rauscher and R. F. Zeigel. Science 144:1144-1147, 1964.

Rauscher leukemia virus (R-NC1-2) was prepared from pooled plasma of viremic BALB/C mice infected 20-30 days previously so that 1 ml of the final virus stock was derived from an initial 10 ml of plasma. Stock samples of virus and non-inoculated controls were layered on the surface of preformed density gradients of appropriate salts and centrifuged at 36,000 rpm. The virus separated into a single band using CsCl, RbCl, sucrose, potassium citrate or potassium tartrate; recovery was particularly high with short centrifugations in potassium citrate. However, prolonged exposure to conc. soln. of potassium citrate caused lysis of the virus.

- 64-731 STUDIES ON VIRUS-CHROMOSOME RELATIONSHIPS. II. DETAILED KARYOTYPES OF MACACA IRUS, ERYTHROCEBUS PATAS AND CERCOPITHECUS AETHIOPS SABAEUS. (Fr.) Pruniéras, M. (Lab. Hyg. Fac. Med. Lyon, France) and C. Chevalier. Ann. Inst. Pasteur (Paris) 106(5):714-726, 1964.

In the course of studying the effect of SV40 on monkey kidney cells in culture, a detailed re-

port is made of the karyotypes of kidney cells of M. irus (42 chromosomes), E. patas (54 chromosomes) and C. aethiops sabaeus (60 chromosomes) in primary cultures in a medium consisting of lactalbumin hydrolysate and calf serum in Hanks' soln.

- 64-732 KARYOTYPE AND POLYOMA VIRUS SENSITIVITY IN CLONES ISOLATED FROM A POLYOMA-INDUCED MOUSE TUMOR. (E.) Hellström, K. E. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Sweden), I. Hellström and H. O. Sjögren. J. Nat. Cancer Inst. 32(3):635-643, 1964.

A karyological study was made on 14 tumor lines established from single-cell clones and isolated from a polyoma-induced mouse tumor (SES0 sarcoma). The tumor lines differed from each other in sensitivity to the cytopathogenic effect of polyoma virus (PV). The resulting data suggested a relationship between karyotype and PV sensitivity of the tumor lines studied, indicating that PV sensitivity may vary with cell genotype.

- 64-733 MORPHOLOGY OF FOCI PRODUCED BY STANDARD PREPARATIONS OF ROUS SARCOMA VIRUS. (E.) Purchase, H. G. (Reg. Poultry Res. Lab., East Lansing, Mich.) and W. Okazaki. J. Nat. Cancer Inst. 32(3):579-589, 1964.

The morphology of the foci of six Rous sarcoma virus preparations, obtained from 3 different sources (2 RPL; 3 Bryan; 1 Popken) and titrated in chick embryo tissue cultures under identical conditions, was compared. The virus preparations were divided into 3 groups according to the morphology of the foci and the presence or absence of "giant cells". Only Bryan CT916 ("high titer strain") and Bryan CT895 preparations produced "giant cells". The possible origin of the differences in morphology is discussed. Since the titrations reported were run under identical conditions, it is concluded that morphological differences in transformation are due to variations in the viral genome and are not differences in the cells affected.

See also abstract nos.: 605,609,610,672,679

EPIDEMIOLOGY AND BIOMETRY

4-734 FOUR HUNDRED CASES OF ORO-PHARYNGO-ESOPHAGEAL CANCER. DENTAL STATE AT THE TIME OF DETECTION. (Fr.) Dargent, M. (Ctr. Leon-Berard, Lyon, France) and P. Bertoin. Ann. Odonto-Stomat. 20(4):181-186, 1963.

In a study of 400 untreated pts. (age 40-70 yr.) with various cancers of the mouth, laryngopharynx or esophagus, only 115 had healthy sets of teeth, 100 had multiple dental cavities, 60 had significant pyorrhea, 54 had pyorrhea + caries, 71 were dentulous and 3 had lesions caused by dentures (1 mouth floor, 1 tongue, 1 gingiva). Results show that while teeth are usually healthy in pts. with cancer of the oral cavity and parotid gland, they are usually in very poor condition in those with cancer of the gingiva, mandible (max. incidence of pyorrhea) and esophagus (max. incidence of multiple caries; no healthy sets of teeth noted in all 21 cases). Only 0.75% of cancer pts. had dental prostheses. The authors stress the possible etiologic significance of these findings.

4-735 ROUTINE GASTRIC EXAMINATION WITH THE USE OF THE GASTROSCOPE. (Jap.) Higashi, K. (Dept. Int. Med., Nihon U., Japan) and S. Tanaka. Rinsho Hoshasen (Clin. Radiol.) 19(9):647-654, 1963.

Routine gastroscopic examination was made of 975 volunteers over age 40; where indicated, additional studies, including biopsy, were performed. In 5 cases there was evidence of gastric cancer (2 cancer, 2 probable cancer, 1 linitis plastica); 6 showed gastric polyps; 349 were essentially normal.

4-736 CANCER CONTROL IN PUERTO RICO. (E.) Marcial, V. A. (Puerto Rico Nuclear Center, Rio Piedras). Radiol. Clin. (Basel) 11(1):39-46, 1964.

Puerto Rico for the year 1960, 1,975 cancer deaths (total population = 2,358,000) were reported (mortality rate = 83.8 deaths/100,000 people) and 3,519 new cases were reported (incidence rate = 152/100,000 people). There was a high incidence of cancer of the cervix, uteri, stomach, esophagus, base of the tongue, and skin; incidence was low for cancer of the breast, major salivary glands, lower g.i. tract and testis. Lung cancer has shown a 100% increase in the last 10 yr. Cancer of the cervix, esophagus and penis are more prevalent in the low income group, while cancer of the breast, endometrium and prostate, are more frequently seen in the well-to-do.

4-737 THE COURSE AND PROGNOSIS OF ULCERATIVE COLITIS. IV. CARCINOMA OF THE COLON. (Eng.) Edwards, F. C. and S. C. Truelove. GUT 15(1):15-22, 1964.

A study of 624 pts. with ulcerative colitis between 1938-62 showed that 22 (3.5%, 8/251 male, 14/373 female) developed carcinoma of the colon as compared to 3 pts. in a comparable sample of the general population. In 17/22, there were single primary growths and in 5/22 there were two primary growths. In relation to carcinoma of the large intestine, of the 27 separate carcinomas, 6 (22.2%) were in the rectum, compared to 36%-40% in the total population for this site. There were 5 cases of colon carcinoma (from the total of 22) reported in pts. between 45-49 yr. and no more than 3 in any other age group (4-yr. intervals; 20-24 up to 70-74 yr.). Of 505 pts. with chronic intermittent attacks and 48 with chronic continuous attacks of colitis, 15 (3.0%) and 6 (12.5%), resp., developed carcinoma. Where colitis extended throughout the entire colon (236 cases), 17 (7.2%) developed carcinoma and where colitis did not involve the entire colon (388 cases), 5 (1.3%) developed carcinoma. The incidence of carcinoma of the colon in relation to age at the onset of ulcerative colitis was less than 5% in those pts. between ages 10-60+, while in those between ages 0-9, the incidence was 12.5% (2/16); none of the 56 pts. aged 60 or more at the start of colitis developed cancer. Of the 109 pts. who had had ulcerative colitis for more than 20 yr., 6 (5.51%) developed colon carcinoma and 7/195 (3.9%) pts. who had had colitis for up to 19 yr. developed carcinoma. In the whole series of 624 pts., 47 had a severe first attack of colitis, 67 had a moderate attack and 136 had a mild attack; of these pts., 4.3% (2), 3.0% (2), and 0% developed colon carcinoma, resp.

64-738 CANCER OF THE STOMACH AND ESOPHAGUS. (Rus.) Isakhanov, P. M. (Regional Dispens. Oncology, Moscow). Sovet. Med. 27(2):49-54, 1964.

Among 32,625 cases of malignant neoplasms, registered in the Moscow region during 1957-1961, incidence of carcinoma was 95.4%. Most frequent site was the stomach (37.6% of all cases) with a rate (per 100,000) of 47.3. Esophageal carcinoma (6.64%, rate 8.5), however, was in sixth place (after uterus, skin, lung and breast). Average annual rates for stomach carcinoma in urban and rural areas was 51.6 and 40.4, resp.; a similar difference was seen for esophageal carcinoma. However, these rates are decreasing: for stomach carcinoma for 1957 and 1961 they were, resp., 28.1 and 12.3; for esophageal carcinoma 24.2 and 11.7. For stomach and esophagus carcinoma, resp., av. annual rates (per 100,000 of the same sex) for men were 53.6 and 10; for women 41.6 and 6.9. The decreases in g.i. cancer were at the expense of the population over 50 yr. of age. Frequency of stomach and esophagus cancer, resp., in pts. under age 29 was 1.2% and 0.6%; in those over age 50, 76.9% and 90.7%. Relative to deaths from neoplasms during the 5-year period, stomach carcinoma occupied first place while deaths due to esophageal

cancer (which early in the period was in 2nd place) during the last 3 yr. was in 4th place (after bronchus, lungs, and pleura, and uterus).

- 64-739 FAMILIAL INCIDENCE OF CANCER. (Ger.) Hörnecke, A. (Robert-Rössle Clin., German Acad. Sci., Berlin) and H. Berndt. Munchen. Med. Wschr. 106(8):336-342, 1964.

The family histories of 780 cancer pts. and 413 control subjects were checked for incidence and location of malignancies. While the overall incidence of cancer was approx. the same in both groups, pts. with carcinoma of the breast, stomach, or cervix reported a higher frequency than statistically expected of these tumors in their immediate families (parents and siblings). This was not true of bronchogenic carcinoma; in the case of carcinoma of the colon, the number of subjects was too small to be conclusive. This preferential localization suggests that heredity plays a significant role in the pattern of organ distribution of malignancies rather than in the general predisposition to cancer.

- 64-740 HEPATIC CIRRHOSIS AS A POSSIBLE PRE-CANCEROUS FACTOR. (Fr.) Mogená, H. G. (Clin. Med., U. Madrid, Spain), H. Oliva and J. M. Aroca. Arch. Mal. Appar. Dig. 52(12):1231-1235, 1963.

Of 67 cases of primary cancer of the liver (39 from the Department of Medicine of the University of Madrid and 28 from the Clinical Hospital of the Faculty of Medicine and the Provincial Hospital of Madrid), 48% were associated with cirrhosis. Among the cancers, 77.7% were hepatomas and 22.3% were cholangiomas. In disagreement with the findings of other investigators the incidence of cirrhosis had no relationship with the tumor type. The similarity between the etiology of the two conditions is stressed. The low (2.5%) incidence of liver cancer observed by the authors among 462 pts. with liver cirrhosis is ascribed to the short survival of the cirrhotic pt. which does not allow time for the development of cancer. Four of the pts. with liver cancer (3 hepatomas and 1 cholangioma) had a history of alcoholism; there was associated cirrhosis in 2/4. No cases were associated with Marchand-Mallory's cirrhosis.

- 64-741 FISTULA CARCINOMA ASSOCIATED WITH CHRONIC OSTEOMYELITIS; PATHOGENETIC AND HISTOLOGICAL ASPECTS. (Ger.) Pfarschner, W. (Dept. Surg., Rudolf-Virchow Hosp., Berlin). Deutsch. Med. J. 15(6):200-207, 1964.

Chronic fistulization of osteomyelitic lesions may lead very rarely to malignant degeneration after a latent period of 30-40 yr. In most cases, these tumors are epithelial rather than mesenchymal in origin. The correlations between trauma, regeneration, and chronic irritation on

the one hand, and carcinogenesis on the other hand, are discussed; regeneration and irritation theories are emphasized. A case is reported where an invasive squamous cell carcinoma developed from a tibial osteomyelitic fistula of 54 yr. duration. This case, though not suspicious clinically and radiologically, was proven malignant by histologic examination, and the leg of the 66-year-old woman was amputated.

- 64-742 STOMACH CARCINOMA AND SURGERY OF GASTRIC ULCERS. (Ger.) Becker, T. (Clin. Surg., Friedrich-Schiller-U. Jena, Germany) and E. Freund. Zbl. Chir. 89(13):455-460, 1964.

An analysis of case histories at the Jena surgical clinic covering the period from 1900 to 1962 showed that during that period 38 pts. were treated for stomach carcinoma or carcinoma of the anastomosis after resection or gastroenterostomy for gastric ulcer. This number represented 1.23% of the total number of primary gastric carcinomas treated during the same period, or 1.17% of the total number of pts. operated upon for gastric ulcer. The incidence of malignant degeneration was highest after gastroenterostomy, lowest after Billroth II; it is concluded that radical surgery of gastric ulcers (Billroth II) affords genuine protection against subsequent malignant degeneration.

- 64-743 INTERPRETATIONS OF EPIDEMIOLOGIC DATA. (E.) Doll, R. (University Coll. Hosp. Sch. Med., Gower St., London). Cancer Res. 23(10):1613-1623, 1963.

A discussion and review (35 references) on the possible contribution that epidemiology can make to the study of the mechanism of carcinogenesis. Examples included the observation that, after a single exposure to radiation, the incidence of leukemia rapidly rises to a max. and slowly falls; this may indicate that cancers showing similar distribution with age are also due to brief periods of exposure to the agent concerned. Also noted was the fact that prolonged exposure, as occurs with cigarette smoke, gives rise to a continuous increase in incidence which is similar to that seen with most of the common epithelial cancers, i.e., an incidence which increases approx. in proportion to the sixth power of the age. Data was obtained showing the relationship between exposure of epithelial tissue and resulting incidence, and the effect of cessation of exposure and of starting exposure at different ages.

- 64-744 FAMILIAL OCCURRENCE OF BRONCHIAL CARCINOMA. (Flem.) Buytendijk, H. J. (St. Joseph Hosp., Heerlen, The Netherlands) and F. Maesen. Acta Tuberc. Belg. 54(4):503-508, 1963.

Two cases are presented of brothers (38 and 39 years of age) who developed within 6 mo. metastatic bronchial carcinoma. The brothers were the 7th and

8th of 11 children of long-lived parents. A sister had died of pulmonary tuberculosis; an older brother had died of gastric carcinoma; and a younger brother was under treatment at the time of report for a planocellular epithelioma of the tongue. All 7 brothers in the present generation were cigarette smokers, beginning at age 13-14 and averaging 20-25 cigarettes/day in adulthood.

64-745 PREVALENCE AND INCIDENCE OF CARCINOID TUMORS. (Sw., Abstract) Månsson, K. and F. Linell. *Nord. Med.* 71(14):446, 1964.

Among a total of 4,828 pts. autopsied between 1959-62 in Malmö, Sweden, carcinoid tumors were found in the g.i. tract in approx. 1%, in the bronchi in approx. 0.1%. A majority of the former were in the small intestine, with a metastatic frequency of 25%. Only 1/48 pts. with such g.i. carcinoid tumors had been diagnosed clinically. In Sweden, the estimated rate of incidence of g.i. carcinoid tumors found at operation was <1/yr./100,000 population (based on surgical records at Malmö, population 230,000, where the actual rate of incidence was approx. 1 case/10 yr.). Carcinoid tumors found at operation were predominantly in the appendix, in pts. under 40, with surgery indicated by conventional symptoms of appendicitis. Very few carcinoid tumors of the appendix were seen at autopsy, suggesting that their development at other sites is not only slow but frequently asymptomatic.

64-746 DEATHS IN THE JEWISH POPULATION ACCORDING TO CAUSE. FOR THE 2ND QUARTER OF THE YEARS 1962 AND 1963. (Heb.) Harefuah 66(1):39, 1964.

Total deaths among the Jewish population of Israel, according to the Central Office of Statistics, during April to June of 1962 and 1963, amounted to 2,758 (1,416 male (m), 1,342 female (f) and 3,179 (1,652 m, 1,527 f), resp., from all causes. Of these, the deaths from neoplasms (malignant, benign and unspecified, International Classification Nos. 140-239) were, resp., 559 (257 m, 302 f) and 602 (270 m, 332 f), being exceeded in number only by diseases of the heart and circulation (927 and 1,119, resp.). Total deaths from neoplasms are classified as follows: Malignant neoplasms, resp., of stomach were 79 (41 m, 38 f) and 69 (41 m, 28 f); of lung 50 (35 m, 15 f) and 45 (38 m, 7 f); of breast 50 (4 m, 46 f) and 71 (0 m, 71 f); leukemias 44 (26 m, 18 f) and 28 (12 m, 16 f); and unspecified as to malignancy 28 (14 m, 14 f) and 19 (13 m, 6 f).

64-747 IS ANYTHING KNOWN ABOUT THE INCIDENCE OF CARCINOMA OF THE STOMACH IN OCTOGENARIANS? (Ger.) Freudenberg, K. *Med. Welt* (15):896, 1964.

In answer to a letter to the editor, it is stated that no statistics on the actual incidence of stomach cancer are available, but official statistics list malignancies of the stomach as the cause of death as follows: in 1960, the mortality rate in the 80-85 age group, per 100,000 persons of the same age and sex, was 623 males, 476 females; in the 85-90 group, 626 males, 523 females. In the group over 90, the figures are probably unreliable, but indicate 386 males, 396 females. These statistics refer to the German Federal Republic but without Berlin.

64-748 SALIVARY SECRETION OF A, B AND H SUBSTANCES IN GASTRIC CANCER IN JAPAN AND THE U.S.A. (E.) Desai, R. G. (Massachusetts Mem. Hosp., Boston 15), W. P. Creger, R. Shirley, N. Gausepohl and A. Amkraut. *Transfusion* 4(3): 188-194, 1964.

Tests for the determination of salivary blood group substances A, B and H were made on 82 USA whites with histologically proven stomach cancer and 130 controls and 212 Asian Japanese pts. with stomach cancer and 177 controls. Mean tube titer analysis revealed that whites with gastric cancer secreted more H substance than controls ($p < 0.001$) and possibly more A substance ($p < 0.05$). The Japanese with gastric cancer did not show these individual secretory differences from their controls. If data is expressed in terms of ABH secretor and nonsecretor status, then the Japanese with gastric cancer show a higher incidence of secretor status ($p = 0.01$) than do controls, while for whites, the secretor status is less clearly increased in those with gastric cancer ($p < 0.05$). The possible relationship of blood group substance to disease is discussed.

64-749 A CLINICAL STUDY OF 134 MONGOLOID CHILDREN. MONGOLISM AND LEUKEMIA. (Fr.) De Wolff, E. (Child. Clin., Canton Hosp., Aarau, Switzerland). *Ann. Paediat. (Basel)* 202 (Suppl.): 17-22, 1964.

Of 134 mongoloid children, 50% of which were under 1 yr. old, examined at the Children's Clinic of the Aarau Hospital between 1945 and 1961, 5/34 died of leukemia (1/5 of congenital leukemia and 4/5 of paramyeloblastic acute leukemia). The frequency of leukemia in mongoloid children (37.5%) was found to be 8-9 times greater than that observed in hospitalized children (4.32%; 45/10,171 pts. in 7-yr. period) at the same clinic. Such a high frequency supports the theory that mongolism and leukemia may have the same origin, inasmuch as both involve abnormal chromosomes.

64-750 TRAUMA AND THE LOCALIZATION OF MALIGNANT MELANOMAS. (Ger.) Holčík, L. (Oncol. Inst., Brno, Czech.). *Derm. Wschr.* 149(15): 378-381, 1964.

Of 343 cases of malignant melanomas only 2.3% (7) were found on the hands (i.e., somewhat less than reported by other authors: 2.7%-3.5%), 1 on the knee, 5 on the neck and 4 on the head. None were found on the elbows. Of the 147/343 pts. from the city, 19.7% had malignant melanomas on their feet; among 196/343 from the country, 15.3% had tumors in the same sites. Among 102 manual workers, 18 (17.6%) had tumors on the feet, compared to 6/47 (12.8%) of white collar workers; the above difference was not statistically significant. Also statistically non-significant were differences seen with respect to head and neck melanomas, i.e., body portions exposed to sun: 31/147 for city dwellers (21.1%), against 41/169 pts. from the country (20.9%). The author concludes that traumatization and/or exposure seem to be of minor importance in the etiology of malignant melanomas.

- 64-751 POSSIBLE RELATIONSHIP BETWEEN TRAUMA AND LEUKEMIA. (It.) Marabini, B. (Dept. Med., Civil Hosp., Rimini, Italy), G. Renzi and B. Bartolan. *Riv. Crit. Clin. Med.* 62(4-5):229-248, 1962.

After reviewing 72 cases from the previous literature regarding the relationship between trauma and leukemia (28 references), the authors present 4 personal cases. Pt. A, male, age 55 yr., had fracture of the left tibia, and 4 ribs and trauma of the spleen and left thorax, with onset of symptoms of chronic lymphoid leukemia 40 days later. Pt. B, male, age 37 yr., had fracture of the left femur and abdominal trauma, with onset of the symptoms of acute hemocytoblastic leukemia after 5 mo. and death 7 mo. later. Pt. C, male, age 35 yr., with thoraco-abdominal trauma, fractured right forearm and spleen rupture followed by splenectomy, with onset of symptoms of acute lymphoreticulosis after 40 days. Pt. D, male, age 17 yr., had fracture of the left wrist, with onset of symptoms of myeloid type leukemoid reaction after 6 mo.

- 64-752 SAMPLINGS AND MEASUREMENTS IN ATMOSPHERIC HYGIENE. (Ger.) Hettche, O. *Zbl. Bakt. (Orig.)* 191(1-3):287-300, 1963.

Different technics of air sampling and pollution measurement are discussed, and the difficulties, as compared to water sampling, are pointed out by various examples. Measurements of 3,4-benzpyrenes in the atmosphere of Hamburg showed values (per 1000 m³) of about 10 µg in summer compared to maximal values of 336 and 482 µg in the winters of 1961 and 1963, resp., with fairly constant total dust samples of 0.16 to 0.32 g. The corresponding 1,2-benzpyrene values were 94% and 50% of the maximal winter figures, resp. The F values (the ratio of 1,2-benzpyrene/3,4-benzpyrene x 100) are given for various locations and for soots of various origins. As against an av. F-value of 66 for dust soot found in English

garages, the mean value for that in outdoor air in English cities was 60; Hamburg, Germany (5 two-month av.), 49.8-93.7; in communities at the edge of the Ruhr District (3 two-month av.), 89.7-91.2; for the Ruhr proper (3 two-month av.), 103.7-108.7. The highest F-value reported was for soot gathered from the outdoor air of Hamburg in February, 1962 = 160.6; contrasting with 80.5 in soot from oil heaters, 154.5 in that from Diesel engines, and 169 in that derived from coal.

- 64-753 PLACE OF MASS RADIOGRAPHY IN RELATION TO LUNG CANCER IN MEN. (E.) Posner, E. (Stoke-on Trent Mass Radiography Unit, England), L. A. McDowell, K. W. Cross, G. P. Bardsley, A. G. Evans, J. T. Hutchison and R. J. Posner. *Brit. Med. J.* 2:1156-1160, 1963.

In Birmingham during 2 periods between July 1955 to June 1960, 310 cases of lung cancer were detected by routine radiographic surveys among 840,694 men (rate, 0.004%) compared to 1,389 cases found by general practitioners among 151,149 (rate, 0.92%). It was concluded that mass radiography does not improve the case-finding rate for cases with favorable prognosis and that serial chest X-rays of men in the critical age groups should be introduced on a large scale.

- 64-754 LEIOMYOMAS OF THE SKIN. (E.) Fisher, W. C. (William Beaumont Gen. Hosp., El Paso, Texas) and E. B. Helwig. *Arch. Derm. (Chicago)* 88(5):510-520, 1963.

Of 38 pts. with cutaneous leiomyomas (29 with multiple lesions), 7 indicated that other members of their immediate families had multiple cutaneous leiomyomas. One fraternal twin brother had tumors on the face, chest, and the shoulder, while the other brother had tumors on the shoulder and back. Three of the family histories showed convincing descriptions of affected relatives, while 2 of them were less lucid.

- 64-755 CANCER CONTROL PROGRAM IN CROATIA. (E.) Spoljar, M. (Inst. Oncol., Zagreb U. Sch. Med., Yugoslavia) and Z. Kulčar. *Med. J. (Lijecn. Vjesn.)* 84(10):1-9, 1962.

The percentage of deaths in Zagreb for 1960 was 22.3, double that of 1939. The rise in frequency was probably due to improved diagnosis, as well as actual increased incidence. Treatment is successful in about 1/3 of pts. with malignant neoplasms. Of 2205 male deaths from cancer in 1960, the most frequent sites (percentage) were: stomach 25.5%; bronchi and lungs 20.7%; leukemia 8.1%; prostate 7.0%; larynx 3.3%; esophagus and urinary bladder 2.8%; pancreas 2.7%; oral cavity, pharynx and intestine 2.5%; rectum 2.1%; other 20.0%. In 2103 female deaths, the sites were: stomach 21.8%, uterus 19.3%, breast 10.6%, leukemia 5.5%, bronchi and lungs 4.6%, intestine 3.6%; ovary 3.5%; rectum

2.9%; pancreas 2.3%; other 26.0%. In 3,776 men and 4,375 women hospitalized in 1960 for cancer, the following sites (percentage) were most frequent, resp.: stomach 15.3 and 9.1; bronchi and lungs 14.0 and 1.9; leukemia 12.0 and 7.0; oral cavity and pharynx 8.1 and 2.2; skin 7.6 and 6.1; rectum 2.9 and 2.7; other 23.3 and 20.2. In men the most frequent sites were: prostate 5.6, larynx 5.8, urinary bladder 3.1 and pancreas 2.3; in women, cervix uteri 22.3, breast 15.0, corpus uteri 7.0 and ovary 5.5. A discussion of cancer control in Yugoslavia follows.

4-756 CHRONIC LYMPHOCYTIC LEUKEMIA OR LYMPHOMA AND CARCINOMA OF THE COLON. CORRELATION WITH BLOOD TYPE A. (E.) Hyman, G. A. (Coll. Phys. Surg., Columbia U., New York), J. E. Altman and C. A. Slanetz, Jr. *J.A.M.A.* 186(12): 1053-1056, 1963.

Among 1,780 pts. with carcinoma of the colon and 650 pts. with leukemia or lymphoma, there were 21 instances where carcinoma of the colon and leukemia or lymphoma occurred in the same pt.; 18/21 pts. had the lymphocytic form of chronic leukemia or lymphosarcoma. Of 20/21 pts. who had their blood group determined, 13 were of blood type A and 18/20 had a D positive Rh group. The incidence of blood type A (65%) in this group was far greater than its incidence in the normal population of the city of New York (35%), the blood donor group of Columbia-Presbyterian Medical Center (36.8%), pts. with carcinoma of the colon alone (38.7%) and pts. with leukemia and lymphoma alone (34%).

4-757 THE GEOGRAPHICAL PATHOLOGY OF PRIMARY LIVER CANCER. (E.) Higginson, J. (Dept. Path., U. Kansas Med. Ctr., Kansas City). *Cancer Res.* 23(10):1624-1633, 1963.

In a review (114 references) of recent epidemiological data on primary liver carcinoma, the incidence of liver cancer (rate/100,000) in U. S. white, U. S. nonwhite, Johannesburg, Mozambique and Uganda males in the following age groups was: <15 yr., 0.2, 0.4, 0.6, 15 and not stated; 15-25 yr., 0.2, 0.0, 2.0, 114 and 1.6; 25-35 yr., 0.3, 2.2, 10.0, 156 and 8.6; 35-45 yr., 0.8, 3.1, 22, 27 and 11.8; 45-55 yr., 4.4, 13.0, 37, 101 and 8.9; 55-65 yr., 21.1, 16.0, 45, 111 and 3.7; 65-75 yr., 23.5, 16.2, 127, 53 and 15.2; 75+ yr., 38.3, 2.4, 59, not stated and 13.9, resp. A less marked but definite increase as compared with the U. S. was also observed in African females. It has been shown that the increase in liver cancer in Africa and Asia was dependent on an increase in the proportion of cirrhotic livers which become malignant rather than on an increased incidence of cirrhosis. Although the pathogenesis of liver cancer in man is unknown, it may be due to liver damage in childhood, possibly from malnutrition, which may predispose the organ to a carcinogenic stimulus in later life; this stimulus may be viral

hepatitis. The effect of trace elements such as iron deposits, native drugs, toxic agents and endogenous liver carcinogens on liver cancer in the African and Asian is also discussed.

64-758 THE INFLUENCE OF A CYTOLOGICAL SCREENING PROGRAM UPON THE INCIDENCE OF INVASIVE SQUAMOUS CELL CARCINOMA OF THE CERVIX IN BRITISH COLUMBIA. (E.) Bryans, F. E. (Dept. Obstet. Gynec., U. Brit. Columbia, Vancouver, Canada), D. A. Boyes and H. K. Fidler. *Am. J. Obstet. Gynec.* 88(7):898-906, 1964.

The relationship of preclinical squamous cell carcinoma of the cervix to the clinical invasive disease, based on data gathered over the past 14 yr., is summarized. Of 381,729 cases screened between 1949-62, detection of in situ, in situ + microinvasion and occult invasive squamous cell carcinoma of the cervix was effected in 1,350, 95 and 65 pts., resp. The mean ages of pts. with in situ, microinvasive foci + in situ, microscopically invasive and clinically invasive squamous cell carcinomas of the cervix were 42.3, 46.2, 50.4 and 52.1 yr., resp. The incidence (number of pts./100,000 population) of clinically invasive, clinically invasive + occult invasive and clinically invasive + occult + in situ with microinvasion squamous carcinomas of the cervix uteri in women over 20 yr. old was 15.5, 18.1 and 22.3, resp., for 1962 as compared to 28.4, 28.8 and 29.8, resp., for 1955. The number of cases of clinically invasive carcinoma in 1961 was 5/146,800 among those screened and 110/339,600 among unscreened pts.; in 1962 these figures were 7/201,600 (screened) and 71/294,000 (not screened).

64-759 PART I: PREVALENCE AND TYPES OF CANCER IN DOMESTIC ANIMALS: COMPARATIVE ONCOLOGY. OCCURRENCE AND TYPES OF TUMORS IN LARGE DOMESTIC ANIMALS. (E.) Moulton, J. E. (U. California Sch. Veterin. Med., Davis). *Ann. N. Y. Acad. Sci.* 108(Art. 3):620-632, 1963.

A review (65 references) is presented, citing the differences and occurrence of tumors in large domestic animals: epithelial tumors are common in cattle, yet absent in the pig; connective tissue tumors are common in horses; embryonal nephroma is one of the most common in pigs, but rare in other species. Skin papilloma or carcinoma and lymphosarcoma are found in most all species, the last being particularly prevalent in the bovine. Tumors which are rather common in man but rare in domestic animals are: mammary and testicular neoplasms, intestinal, bile duct, prostatic and bronchogenic carcinoma, rhabdomyoma and radiation-induced neoplasm. The possibility of viral etiology (cattle carcinoma of the urinary bladder, skin papillomas, lymphosarcoma and "cancer eye") and hereditary predisposition ("cancer eye" and lymphosarcoma) as well as the influences of geographical factors, age, breed, sex and site of tumor are discussed.

- 64-760 STATISTICAL REVIEW OF CANCER DETECTION WORK IN HUNGARY, BASED ON 4.5 MILLION SCREENING TESTS. (E.) Vicol, J. (Centl. Oncol. Inst., Budapest, Hungary). *Acta Un. Int. Cancr.* 19(5):885-887, 1963.

An organized cancer detection program conducted in Hungary for the past 10 yr. (screening women over 30 yr. of age) has led to the detection of about 20,000 malignant growths. Since the initiation of this program, a decrease in deaths from uterine cancer (expressed as percentage of female deaths from all cancers) has been seen (from 21.1% in 1954 to 17.2% in 1961). In one year, of 563 pts. treated for established precancerous states, only 30 (5.3%) developed malignancies (cervix uteri 18, other gynecological sites 2, breast 9 and skin 1).

- 64-761 HEPATOMA IN CIRRHOSIS. (E.) Elkington, S. G. (St. Thomas's Hosp., London), D. J. McBrien and H. Spencer. *Brit. Med. J.* 2:1501-1503, 1963.

Among 7,366 necropsies performed at St. Thomas' Hosp., 1940-62 there were 39 cases (0.53%) of primary hepatic carcinoma and 157 cases (2.13%) of cirrhosis. The total incidence of primary hepatic carcinoma among pts. with cirrhosis was 19.1%, while an analysis by 4-year periods showed a progressive increase of the rate of incidence (1948-62) from 11.1-28.3%. Active chronic peptic ulcer occurred in 14.2% of the pts. with cirrhosis and in 23.3% of those with primary carcinoma of the liver. The incidence of primary carcinoma of the liver at necropsy in Europe and the USA is reviewed (16 references). It is concluded that primary hepatic carcinoma among pts. with hepatic cirrhosis appears to be more common than generally supposed.

- 64-762 THE ABO BLOOD GROUPS IN NEOPLASTIC DISEASE OF THE OVARY. (E.) Osborne, R. H. (Sloan-Kettering Inst. Cancer Res., New York) and F. V. De George. *Am. J. Hum. Genet.* 15(4):380-388, 1963.

Blood group distribution (percentage; O, A, B and AB, resp.) in various histologic types of 453 malignant ovarian neoplasms was as follows: 17 pseudomucinous 47.1, 47.1, -, 5.9; 15 mucinous 46.7, 26.7, 26.7, -; 9 cystadenocarcinoma 55.6, 22.2, -, 22.2; 14 serous cystadenocarcinoma 42.9, 42.9, 14.3, -; 20 anaplastic adenocarcinoma 45, 40, 15, -; 103 adenocarcinoma 52.4, 37.9, 7.8, 1.9; 234 papillary adenocarcinoma 35.9, 46.6, 12.0, 5.6. Among malignant ovarian neoplasms, significant excesses of papillary adenocarcinoma (ratio 1.44) and secondary carcinoma (ratio 6.10) were found in women with Group A blood. Since these findings agree with a similar study on salivary gland tumors, the authors suggest a blood Group A association with some premalignant process.

- 64-763 EWING'S SARCOMA IN SIBLINGS. REPORT OF THE SECOND KNOWN OCCURRENCE. (E.) Hutter, R. V. P. (Dept. Path., Memorial Hosp. Cancer Allied Dis., New York), K. C. Francis and F. W. Foote, Jr. *Am. J. Surg.* 107(4):598-603, 1964.

This report is the second documented occurrence of Ewing's sarcoma in siblings. The pts. reported were the 2nd and 3rd of 3 sisters whose maternal grandfather died of recurrent carcinoma of the colon and whose mother underwent unilateral radical mastectomy for a ductal carcinoma of the breast. The youngest sister was first treated at the age of 3 1/4 yr. for Ewing's sarcoma of the left 6th rib, metastasized to the pleura, approx. 2 mo. after symptoms appeared; she died 13 mo. after initiation of treatment with X-rays, chemotherapy and surgery. Nine yr. later, the 2nd sister (now aged 16) developed Ewing's sarcoma of the left 5th metatarsal. After approx. 16 mo. remission in response to X-ray + chemotherapy, recurrence was resistant to similar treatment and the leg was amputated below the knee. At the time of report, the pt. had been symptom-free for approx. 6 mo. post surgery.

- 64-764 A CERVICAL CYTOLOGY SCREENING PROGRAMME IN THE THAMES AREA. (E.) McIndoe, W. A. *New Zeal. Med. J.* 63(377):6-13, 1964.

A cervical cytology screening program has been in operation for 1 yr. in the Thames area of New Zealand, during which time 2,817 pts. (41% of the population in the age group of 25-69 yr.) have been examined. The total number of cervical smears prepared was 3,098 (approx. 10% were repeats). The following positive cytological diagnoses were made in 24 cases (age 28-67 yr.; parity 1-6; biopsy confirmation in 23/24): 4 invasive carcinoma of cervix; 14 cervical carcinoma *in situ*; 5 cervical dysplasia; 1, no biopsy obtained. Presently, 62 cases of atypical cells are still being followed. At this point in the program it would appear that the most dangerous age group is 35-44 yr., and that the "pick-up rate" is higher (6.39/1000) in this region than previously reported.

- 64-765 ON THE PREVENTION OF CARCINOMA OF THE CERVIX. (E.) Elliott, R. I. K. (Royal Sussex County Hosp., Brighton, England). *Lancet* 1:231-235, 1964.

In a review (45 references) of statistical data taken from the Registrar General on mortality rates from carcinoma of the uterine cervix at all ages in England and Wales, a steady decrease (per million) was seen from 117 in 1950 to 104 in 1954; a transient increase developed from 1955-61 with highs of 116 in 1958 and 110 in 1960. The fall in mortality has affected chiefly younger age groups, while rates for older women have declined very little. That social factors play a determining role is shown by the fact that wives (aged 20-64) of clergy, doctors and lawyers have

standardized mortality rates of 18, while wives of bricklayers and laborers have mortality rates as high as 233 for the same age group. Higher incidences of cervical carcinoma were seen in married women, in women married more than once, in promiscuous women, in women starting intercourse early in life and in Jewish women. Cleanliness, freedom from the weak carcinogenic effect of megma and the use of contraceptives are advocated by the author for the prevention of cancer of the cervix.

4-766 PRIMARY LIVER CARCINOMA IN THE PHILIPPINES. AN ANALYSIS INTO ITS ETIOLOGIC FACTORS AND PATHOGENESIS. (E.) Almacio-Cruz, A. E. (Dept. Path., U. Philippines Coll. Med., Diliman, Quezon City). J. Philipp. Med. Assn. 39(12):928-949, 1963.

Statistics at the Philippine General Hospital (4 cases were from other hospitals) from 1953-1962 indicated that of 80 pts. (63 males, 17 females) with carcinoma of the liver, 58 (72.5%) were preceded by cirrhosis, while 22 (27.5%) appeared in non-cirrhotic livers, all but 1 showing evidence of hepatofibrosis. Histologically, 90% of liver cancers were of the hepatocarcinoma type; 10% were pure or mixed cholangiomas. Of 130 pts. with post-necrotic and "portal" cirrhosis, 58 (44.6%) were associated with primary liver carcinoma, while 1 had metastases from a gastric carcinoma. The male:female ratio for cirrhosis with/without liver cancer was 3.2:1; for cirrhosis without cancer, 2.1:1; cirrhosis with cancer, 6.3:1; cancer without cirrhosis, 1.4:1; cancer with/without cirrhosis, 3.7:1. The av. age range in both sexes was 43.9-46.7 yr. Vitamin A and riboflavin deficiency, hyperestrinism and crude herbal alkaloids as possible carcinogenic linking factors are considered. The relationship of schistosomiasis, fatty liver changes, hepatitis, peptic ulcer, tuberculosis, alcoholism, malnutrition and malaria to cancer and/or cirrhosis is discussed. The most frequent triad of sequence was found to be viral hepatitis, post-necrotic cirrhosis and liver carcinoma.

4-767 CARCINOMA OF THE BLADDER IN SOUTHERN RHODESIA. (E.) Houston, W. Brit. J. Urol. 36(1):71-76, 1964.

52 cases (0.1% of all admissions) of carcinoma of the bladder (40 males, 12 females) seen at Pietermaritzburg General Hosp. in Southern Rhodesia from September 1, 1961 to August 31, 1963, the age range was 25-80 yr. (av. 52 yr.) for males and 25-80 yr. (av. 49 yr.) for females. On first attendance 31 pts. had a palpable mass with extravasical spread, 10 had distant metastases, 5 had mobile tumors, and in 6 no definite mass was palpable. In relation to bilharziasis, histologic types and number of these sections containing ova were, resp., as follows: squamous carcinoma 27/52 and 8; anaplastic carcinoma 9/52 and

3; transitional cell carcinoma 5/52 and 3; adenocarcinoma 2/52 and 1; unspecified carcinoma 3/52 and 0; not examined histologically 6/52 and 0. Two factors in this study, which seem to apply where bilharziasis is endemic, can be adduced in favor of a causal connection between bilharziasis and cancer of the bladder: the early age at which the cancer appears (50% of males and 77% of females were <50 yr. old) and the high proportion of squamous cell types as compared with findings in Europe and North America. A possible genetic factor is also considered.

64-768 THE FIGHT AGAINST CANCER IN THE GERMAN DEMOCRATIC REPUBLIC. (Ger.) Held, F. (Clin. Radiol., U. Rostock, Germany). Sante Publique 6(2):147-161, 1963.

The compulsory notification method for all suspected and confirmed cancer cases in East Germany was described, followed by a statistical analysis of 250,000 cancer cases reported since 1953-1958, according to age, sex, location and type. In a predominantly agricultural region, the number of lung cancer cases was 11.2/100,000 as compared to 21.2/100,000 cases in an industrial region. The increase in lung cancer was also shown by the following: the number of cases of bronchial cancer in 1953 and 1954 was 2,814 and 3,138, resp., while in 1958, there were 4,500 cases (i.e., 7% in 1953; 7.6% in 1954; and 9.5% in 1958, resp., of all reported cancer cases). Divided by sex, the percentage of men with bronchial carcinoma in 1953, 1954 and 1958 was 15%, 15.9%, and 19%, resp., of all men with carcinoma, while the percentage for women was 1.4%, 1.5%, and 1.9%, resp. Only 7-8% of these cases could undergo radical surgery, while only 1% of bronchial carcinoma cases of 1953 were alive after 4 yr. The overall 5-yr. cancer survival time (calculated from the East Berlin sector) was 22%. It was emphasized that early recognition of cancer could increase the 5-yr. survival av. to 40%.

64-769 STOMACH CANCER AND ADRENOCORTICAL HYPERFUNCTION. (E.) Card, I. (Royal Hosp., Sheffield, England) and D. Mullan. Lancet 1:940-941, 1964.

The authors present the case of a 66-year-old man admitted to the hospital with gross malignant ascites, finger-clubbing and mild diabetes mellitus. Necropsy revealed a large adrenocarcinoma (8 cm in diameter) of the lesser curve of the stomach with peritoneal deposits, invasion of the para-aortic glands and a single hepatic metastasis. Extensive adrenocortical hyperplasia was seen histologically, but there was no evidence of secondary deposits.

64-770 ADENOCARCINOMA OF THE SMALL INTESTINE OCCURRING IN A CASE OF REGIONAL ENTERITIS. (E.) Berman, L. G. (Dept. Surg. Path., State U. New York, Syracuse) and J. T. Prior. J. Mount Sinai Hosp. 31(1):30-37, 1964.

A case history of a 51-year-old man is presented showing an association between adenocarcinoma of the small intestine and chronic regional enteritis. Histologic examination revealed ulcerated areas in both the large and small bowel with a large zone of mucosal polypoid hyperplasia in the ileum in which a well-differentiated adenocarcinoma could be seen extending through all coats of the bowel into the serosa. A review of 6 other cases (8 references) of this association is presented.

- 64-771 ONE THOUSAND CASES OF LUNG CANCER. (E.) Perrone, J. A. (Mercy Hosp., Pittsburgh, Pa.). Penn. Med. J. 67(4):31-34, 1964.

After reviewing the literature on lung cancer incidence, the author presents a review of 1,000 of his own proven cases of bronchogenic cancer (784 male, 216 females; 754 whites, 246 nonwhites). The disease was still found to be predominant among males (in spite of increased smoking in women for the past three decades), occurring mostly during the 4th, 5th, and 6th decades of life. The author's series showed a much larger percentage (approx. 2.5-3.5 times higher) of lung cancer cases in those exposed to irritating gases and a high degree of air pollution (bus operators, steel workers, etc.) than in doctors, dentists, and lawyers. For all pts., carcinoma types for nonsmokers and smokers were as follows: squamous cell 241 and 336; undifferentiated 83 and 97; adenocarcinoma 31 and 44; oat cell 47 and 62; mixed 22 and 37, resp. In nonsmokers and smokers, carcinoma types in females and males were as follows: squamous cell 93 and 285; oat cell 18 and 103; undifferentiated 78 and 166; adenocarcinoma 22 and 58; mixed 5 and 72. In spite of the increased incidence of bronchogenic carcinoma, there has been no proportionate increase in the occurrence of upper respiratory cancer, thus making smoking a questionable etiological factor.

- 64-772 PRENATAL ORIGIN OF CHILDHOOD LEUKEMIA. EVIDENCE FROM TWINS. (E.) MacMahon, B. (Dept. Epidemiol., Harvard Sch. Med., Boston, Mass.) and M. A. Levy. New Eng. J. Med. 270(21): 1082-1085, 1964.

Investigation of 72 sets of twins with leukemia in at least one member and assembled from 4 statistical sources revealed the existence of 5/72 sets of twins with leukemia in both members. Sex distribution was male-male in 2/5 and female-female in 3/5 sets of twins affected; concordance rate for like-sex sets was 1:9, a figure much higher than that currently recognized. Definitive information about zygosity was available for only 2 pairs, but it seems probable that all 5 pairs were homozygous. If it is true that the observed concordance of like-sex sets results from concordance of monozygous sets, it would appear that approx. 25% of the monozygous twins of pts. affected will themselves be affected.

- 64-773 MATERNAL DEATHS DUE TO TROPHOBLASTIC TUMORS. (E.) Baken, M. P., Jr. (4959 Excelsior Blvd., Minneapolis 16, Minn.). Minnesota Med. 47(4):447-455, 1964.

A study dealing with maternal deaths due to trophoblastic tumors in Minnesota is presented. Of 3,413,864 live births reported from 1950-61, there were 14 deaths (1 fatality/70,000 live births) due to maternal choriocarcinoma and/or chorioadenoma destruens. Over 70% (11/14) of the cases were 28 yr. of age or less and over 50% (8/14) were 25 yr. of age or less. As to number of previous pregnancies, there were 7 with none, 1 with 2 previous pregnancies, 3 with 3, 1 with 4. The incidence of the type of pregnancy preceding development of choriocarcinoma was: term pregnancy (28.6%), abortion (35.7%), hydatidiform mole (28.6%), with one case thought to represent an ab initio choriocarcinoma of the ovary. Nine (64%) of the 14 cases died of their disease in <1 yr. after its onset; 12 (86%) were dead within 24 mo.

- 64-774 INTRA-ABDOMINAL MALIGNANT LYMPHOMAS IN AUTOPSIES AT KORLE BU HOSPITAL, ACCPA. (E.) Younn, S. S. (Natl. Inst. Health, Ghana Acad. Sci.). Ghana Med. J. 3(1):21-25, 1964.

Of 330 autopsies performed within an 11-mo. period, 23 (7%) were malignant neoplasms, of these 7 (6 males, 1 female; 11-43 yr. old) were cases of intra-abdominal (predominantly gastric and retroperitoneal) malignant lymphoreticular tumors. In all cases there were extensive metastases. Histologically, all the tumors were found to be composed of mixtures of lymphoreticular cells, although the predominant cell type was reticulum cell in 5 cases and lymphoblast in 2. The various nuclear alterations depicted were strongly suggestive of a viral etiology. Attention is drawn to the possible relationship between the jaw tumors in East African children and the lymphoreticular tumors in Accra. It is suggested that these two tumor types may be manifestations of a similar malignant neoplastic process.

- 64-775 INCIDENCE OF DISEASE IN THE NAVAJO INDIAN. A NECROPSY STUDY OF CORONARY AND AORTIC ATHEROSCLEROSIS, CHOLELITHIASIS, AND NEOPLASTIC DISEASE. (E.) Hesse, F. G. (Bernalillo County-Indian Hosp., Albuquerque, N. M.). Arch. Path. (Chicago) 77(5):553-557, 1964.

A study of 87 adult Navajo necropsies (56 males and 31 females above 20 yr. of age) showed a 19.3% incidence (17 cases) of malignant neoplasms, which included the following types of carcinoma: pancreas 3, gall bladder 3, kidney 2, and 1 each stomach, cervix, breast, ovary, bladder, liver, prostate, meningioma and metastatic abdominal adenocarcinoma. Since malignant neoplasms in this study appeared as frequently as in similar non-Indian studies, the author suggests that the

frequency based on more complete studies would be greatly increased. There was a decreased incidence of coronary and aortic atherosclerosis in the group.

4-776 DIETARY FACTORS IN CARCINOMA OF THE STOMACH. A STUDY OF 100 CASES AND 200 CONTROLS. (E.) Acheson, E. D. (Nuffield Dept. Med., Radcliffe Infirm., Oxford, England) and J. Doll. *Gut* 5(2):126-131, 1964.

No differences of etiological importance in the type or quantity of foods, beverages or alcoholic drinks were seen as a result of interviewing 100 pts. under 75 yr. of age with confirmed gastric carcinoma and 200 control pts. (matched for age within 5 yr. in whom gastric and duodenal disease was excluded) and re-interviewing, after 3 mo., 10 gastric cancer pts. and 53 controls. Positive findings, but contrary to current hypotheses, were obtained in answers to questions on the temperature at which food and drink were preferred and the quantity of fried food taken. Cancer pts. preferred food and drinks at cooler temperatures than controls and frying as a method of cooking was employed less than in controls.

4-777 STATISTICAL STUDIES OF BRONCHOGENIC CARCINOMA IN NORDRHEIN-WESTFALEN. (Ger.) Boche, R. (Inst. Path. Med., Acad. Dusseldorf, Germany), O. Mittmann and O. Kneller. *Zschr. Krebsforsch.* 66(1):87-108, 1964.

A more detailed summary of the studies previously reported in CRA 1(3):#528, 1963, adds that the rate of increase of bronchogenic carcinoma in these areas is independent of age group; while the relatively greater frequency of the disorder in males has been accompanied by a compensatory decrease of the relative frequency of other organ tumors, so that the total rate of incidence of malignancies at any given time is approx. equal in males and females. There is no evidence that changes of residence, refugee status, military service, prisoner-of-war experience, cigarette smoking, or changes of occupation play an etiologic role. On the other hand, significant correlations were demonstrable between membership in occupational groups exposed to considerable degrees of air pollution, including outside workers exposed to Diesel and other motor fumes.

4-778 GONADOBLASTOMA ASSOCIATED WITH PURE GONADAL DYSGENESIS IN MONOZYGOUS TWINS. (E.) Frasier, S. D. (Dept. Pediat., Ctr. Health Sci., Los Angeles, Cal.), R. A. Bashore and H. D. Frasier. *J. Pediat.* 64(5):740-745, 1964.

Female monozygous twins (age 6 yr.) with pure gonadal dysgenesis, a chromatin-negative buccal smear and a normal male (44A-XY) karyotype both presented gonadoblastomas, with nodules composed of nests and masses of immature germinal and

Sertoli cells surrounded by fibrous connective tissue. This illustrates the relationship of gonadoblastoma to abnormalities of gonadal and genital differentiation. Other possible causative factors are considered.

64-779 MALIGNANT DISEASES IN MELANESIAN CHILDREN. (E.) Ryan, B. (Children's Hosp., Lagos, Nigeria), P. E. Campbell and C. Farago. *Med. J. Aust.* 1(12):436-440, 1964.

Seventeen cases of malignant tumors in Melanesian children (age 4 mo.-12 yr.; 14 male, 2 female, 1 sex not stated), detected over a period of 2 yr. (1960-1961) at the Port Moresby General Hospital, are reviewed. Biopsies revealed the following types: lymphosarcoma 9/17 (1/9 probable); neuroblastoma 4/17; Wilms's tumor 1/17; glioma of the pons 1/17; hemangiosarcoma 1/17; osteogenic sarcoma 1/17. Two cases of leukemia were diagnosed during the period of the survey. Attention was drawn to the similar pattern of malignant disease (predominance of lymphosarcoma over embryonal tumors; high frequency of facial involvement) in Melanesian and African children.

64-780 ALASKA 1963 ORAL CANCER SURVEY. (E.) Smith, R. W. *Alaska Med.* 6(1):5-7, 1964.

In a study of 1,097 pts. (age 1-91 yr.; 44% male, 56% female), 185 oral lesions were reported. Of these, 49% (92) were considered to be precancerous or the result of chronic irritation; it was judged that these required therapy to prevent precancerous changes. Malignant and potentially malignant oral lesions were classified as follows: squamous cell carcinoma 1; epulis fissuratum 9; hemangioma 6; hyperkeratosis 25; hyperplasia 29; leukoplakia 1; linea alba 3; papillomatosis 6; traumatic ulcer 12. Benign lesions were reported in 92 pts. When based on total lesions/hundred, 16.7 and 19.5 were found in females and males, resp. All potentially cancerous lesions were directly related to either physical or chemical trauma; approx. 50% were secondary to the wearing of partial or full dentures.

64-781 THE DECLINING INCIDENCE OF CARCINOMA OF THE STOMACH. (E.) Anderson, M. D. (Georgetown U. Sch. Med., Washington, D. C.) and R. J. Coffey. *Georgetown Med. Bull.* 17(4):201-207, 1964.

In a discussion on the declining incidence of carcinoma of the stomach (28,9/100,000 population in 1930 compared to 13 in 1955), it is suggested that this decrease in the U. S. may be attributed to one or both of the following: (1) The atmosphere is less polluted with the specific type of carcinogen-laden soot particle (containing aromatic polycyclic hydrocarbons, such as 3,4-benzpyrene) formerly produced in abundance by the incomplete combustion of bituminous coal. Presently, the

electric power utilities, which are the largest coal consumers, combust coal completely up to an efficiency of approx. 90%. (2) With the increasing use of cigarettes and increasing air pollution in recent yr., the carcinogenic particles in polluted air are more likely, by virtue of their smaller size, to be transported with the inspired air primarily into the lung instead of being arrested at a level cephalad enough to be expectorated or swallowed.

- 64-782 THE EPIDEMIOLOGY OF GASTROINTESTINAL CANCER WITH SPECIAL REFERENCE TO CAUSATION. (E.) Boyd, J., M. Langman and R. Doll. *Gut* 5(2):196-200, 1964.

The consensus of this demographic study is that the main causes of g.i. cancer arise from the diet; however, the evidence is only suggestive. Gastric cancer is common in Japan, Iceland, Finland, Poland, parts of the USSR, China and Chile; it is relatively rare in the USA (white population) and very rare among native populations in many parts of Africa, S. America and India. Where the staple food is maize, the disease is rare; where it is potatoes, it is common. Esophageal cancer is common in France, Switzerland, Finland, Iceland and the Karelian SSR plus extremely high incidences in localized areas such as the Transkei region of S. Africa, part of the Chinese province of Honan, Curacao and among the Bantu (within the last 30 yr.). Three factors cited as important are tobacco, alcohol consumption and nutritional deficiency. Cancer of the large intestine is particularly common in Scotland and Denmark; rare in Israel and parts of Africa as well as in countries with a high incidence of gastric cancer. No particular factor was cited as a causative agent.

- 64-783 LACTATION AND MENSTRUAL FUNCTION AS RELATED TO CANCER OF THE BREAST. (E.) Levin, M. L. (Roswell Park Mem. Inst., Buffalo, N.Y.), P. R. Sheehe, S. Graham and O. Gildewell. *Am. J. Public Health* 54(4):580-587, 1964.

In an epidemiological study of menstrual activity and lactation in relation to mammary cancer, the factors associated with increased or decreased risk as compared to the general population in a series of mammary cancer pts. seen over yr. 1955-1957 were: artificial menopause, 0.50 risk; lactation for 36 mo. or more, 0.46; never married, 1.07; married but never pregnant, 1.08; married more than once but never pregnant, 1.42; married after age 25 with 1 or more live births, 1.47; first pregnancy after age 25, 1.36; married, pregnant with live births but never lactated, 1.24; nursed less than 36 mo., 1.21. The risk of breast cancer during menstrual years was found to increase 4.9% faster than during postmenopausal

years. The results from pooled admissions between 1955-1959 indicate that with lactation up to 17 mo. the risk of mammary cancer appears to increase, but thereafter it declines until at about 36 mo. or more; the net effect is a reduction of risk to levels which are similar to those previously reported for Japan.

- 64-784 MORTALITY RATES AMONG COAL MINERS. (E.) Enterline, P. E. (Div. Occupational Health, U. S. Public Health Serv., Washington, D. C.). *Am. J. Public Health* 54(5):758-768, 1964.

A study of the mortality rate among coal miners in the United States in 1950 is presented. In those between ages 20-64, the observed number and expected number of deaths, resp., due to various neoplasms were: buccal cavity and pharynx, 21 and 16; stomach, 146 and 53; intestine and rectum, 78 and 59; trachea, bronchus and lung, 161 and 84; prostate, 35 and 17; kidney, 22 and 11; bladder, 24 and 14; leukemia and aleukemia, 30 and 20; lymphosarcoma, 47 and 29. The influence of environmental factors on this high mortality rate in U. S. mines is discussed and compared with Britain where the rate is only one-half as great.

- 64-785 OXFORD SURVEY OF CHILDHOOD CANCERS; PROGRESS REPORT II. (E.) Barber, R. (Dept. Social Med., Oxford U., England) and P. Spiers. *Monthly Bull. Minist. Health (London)* 23:46-52, 1964.

Of 3780 survey children (1,795 leukemias; 1,985 other cancers) and 3778 controls, 270 (7.14%) and 154 (4.08%), resp., were associated with congenital defects while 52 (1.38%) and 1 (0.03%), resp., were associated with mongolism. Of the 53 survey children with mongolism, 49 had leukemia, 3 had other cancers (2/3 lymphosarcomas) and 1 was a control. In 9570 and 9025 mothers of survey and control children, 1026 (10.73%) and 909 (10.07%), resp., miscarried in other pregnancies and 197 (2.06%) and 196 (2.17%), resp., had previous still-born births. Of 8347 and 7920 liveborn sibs of survey and control children, 160 (1.92%) and 141 (1.78%), resp., had a record of congenital defects and of the 401/8347 and 388/7920 who died before the interview date, 29 (0.35%) and 6 (0.08%), resp., died of neoplasms. Of 9725 siblings of survey children, 13 died of leukemia and 18 died of other neoplasms; expected incidences were 4.3 and 3.6, resp. Incidences in all control siblings was 4 and 3, resp. Of 8616 grandparents of survey children and 8524 of control children, 7.2% and 6.9%, resp., died of neoplasms, and of 14677 aunts and uncles of survey children and 14604 aunts and uncles of control children, 0.9% and 0.8%, resp., died of neoplasms. Information was also collected on cousins, however, no reliance is being placed on this information.

See also abstract nos.: 606,607,612,628,685

MISCELLANEOUS

64-786 THE INTERSTITIUM OF EPITHELIAL TUMORS OF THE MUCOUS AND SALIVARY GLANDS. (Ger.) Böck, J. (2nd Eye Clin., U. Vienna, Austria) and F. Feyrter. Zschr. Krebsforsch. 6(1):46-58, 1964.

The intercellular interstitium of so-called mixed tumors of the salivary glands was found to be pathologically altered in its structure, presumably due to the colloidal, mucopolysaccharide-rich nature of its ground substance. The histological changes observed were mucoid degeneration with and without histolysis; deposition of chondrinous ground substance; fibroid degeneration of myxomatous tumors, with an abundance of argyrophilic fibrous masses and subsequent hyalinization; occurrence of trabeculae with peculiar argyrophilic, PAS-positive, fuchsinophilic structures; and occurrence of spidery and circular structures and coacervates. It is suggested that the tumor epithelium itself also takes part in inducing these changes, presumably through hormonal or enzymatic activity affecting the fibroplastic and fibrocytic elements and the vascular walls of the interstitium.

64-787 LOCAL FACTORS AFFECTING TUMOR GROWTH. I. EFFECT OF TISSUE HOMOGENATES. (E.) Fisher, B. (Dept. Surg., U. Pittsburgh Sch. Med., Pa.) and E. R. Fisher. Cancer Res. 23(10):1651-1657, 1963.

Female Sprague-Dawley rats (175-200 g) receiving s.c. inoc. of Walker tumor cells (TC; 500,000 cells) developed 4/47 (9%) tumors on day 18 and 100% on day 20. Concomitant s.c. inoc. of 0.5 ml of 30% rat liver homogenate caused earlier appearance of tumors (32% by day 11; 100% by day 15) and acceleration of growth. Inoc. s.c. of liver homogenates (brain, kidney, skeletal muscle and spleen) also accelerated tumor onset and growth, regardless if heated or frozen or prepared from dog or rabbit. When homogenates were inoc. at different sites (s.c. or i.p.) tumor onset was accelerated, except for i.p. inoc. of spleen homogenate which failed to elicit a response. Intraportal inoc. of 5,000 TC + 30% liver homogenate resulted in 85% tumors on day 15 (as compared to 19% in controls receiving TC alone) and increased lung metastases; TC + 30% spleen homogenate gave 100% tumors. After inoc. of 5,000 TC intraportally, s.c. inoc. of liver and kidney homogenates failed to evoke a response. The inj. of homogenate in one member of a parabiotic pair had a similar growth promoting effect on tumor growing in the other parabiont. Of particular interest was the occurrence of tumor at the site of homogenate inj. in both single and parabiotic animals when this was separate from the location of tumor cell inoc. Suggested was the hypothesis that the tumor growth-promoting factor is the product of dead or dying normal cells rather than a humoral factor associated with regeneration.

64-788 HISTOGENESIS OF GRANULOSA CELL TUMORS. DEMONSTRATED BY AUTORADIOGRAPHY OF OVARIAN TRANSPLANTS INTO THE SPLEEN OF RATS. (Nor.) Myhre, E. Nord. Med. 71(1):8-11, 1964.

In rats of an unspecified strain, bilateral ovariectomy was followed by autologous transplant of one of the ovaries into the spleen; after 17, 49, 100, 175, and 469 days each was given a s.c. inj. of 125 μ C tritiated thymidine 0.75-1 hr. before sacrifice. By the end of the study, essentially autonomous tumor growths had developed in the place of the transplants, but pathological proliferation or other evidences of malignancy were not found.

64-789 UNILATERAL HISTOGENESIS OF AKR THYMIC LYMPHOMA. (E.) Siegler, R. (Albert Einstein Med. Ctr., Philadelphia, Pa.) and M. A. Rich. Cancer Res. 23(10):1669-1678, 1963.

In the preleukemic period, the left and right thymus glands in AKR mice were differentially altered by unilateral perivascular hemorrhages and lymphocyte depletion (lympholysis). The depleted organ became smaller, due to contraction of the epithelial reticulum, and the unilateral loss of cortical lymphocytes. Of 41 cases of thymus lymphoma, 39/41 (95%) showed presence in only 1 thymus; 7/39 showed tumor in the smaller of the two thymuses. The lymphoma invaded the opposite thymus by direct extension, but in two cases a tumor growth in the spleen suggested a systemic dissemination before invasion of the opposite gland. A discussion of the anatomical and cytological alterations of the thymus (24 references) follows.

64-790 GROWTH OF HUMAN TUMOR CELLS IN SUSPENSION CULTURES. (E.) Moore, G. E. (Roswell Park Mem. Inst., Buffalo, N. Y.), D. Mount, G. Tara and N. Schwartz. Cancer Res. 23(11):1735-1741, 1963.

Eight newly established tumor cell lines (1 each of osteogenic sarcoma, gallbladder carcinoma, mesothelioma, liposarcoma, nasal septum adenocarcinoma, carcinoma and adenocarcinoma of the colon; 2 ovarian carcinomas) were grown as suspension cultures in a special incubator. Described are two media which support the growth of human cells in suspension with minimal serum supplements (<1%). Several cell lines have been grown in a simple medium containing insulin and 0.1-0.5% albumin, but without serum. Three cell lines cultured in these media have been growing for more than 100 days. The advantage of the media described is that they support rapid cell growth without requiring repeated gassing or large amounts of serum.

- 64-791 ENDOMETRIAL CARCINOMA ASSOCIATED WITH GRANULOSA CELL TUMOUR OF THE OVARY. REPORT OF A CASE. (E.) Sallam, N. A. (Dept. Obstet. Gynec., U. Alexandria, U. Arab. Rep.). Alexandria Med. J. 10(1):69-74, 1964.

The case history is presented of a 70-year-old multipara with endometrial carcinoma in association with granulosa cell tumor of the ovary and preceded by a 20-year history of postmenopausal uterine bleeding. A review (9 references) of cases reported in the literature and of the relationship between estrogen-producing tumors of the ovary and endometrial hyperplasia and carcinoma follows.

- 64-792 SPONTANEOUS RESOLUTION OF GIANT CELL TUMORS IN LONG BONES. (Rus.) Kvaliashvili, A. A. (Dept. Roentgenol., Acad. Sci. Georgian SSR, Tbilisi), D. G. Mamamtavishvili and M. V. Tatishvili. Khirurgiia (Moskva) 40(5):115-119, 1964.

Spontaneous resolution of trabecular giant cell tumor of the tibia with complete return to normal of the bone structure was observed in one female pt. after 32 yr. Regression of pathological changes due to the lytic form of giant cell tumor of the tibia was observed in one male and one female pt. after 26 and 13 yr. of observation, resp. In another female pt. the spontaneous recovery of giant cell tumor in the humerus came after 18 yr. As reason for this spontaneous reduction of bone tumors, the authors suggest the change in biological properties of tumor cells, and not in the embryonal blood flow as claimed by the theory of A. V. Rusakov. The regression is possible only in young people and can occur in benign fibromas and papillomas as well as in any primary malignancy.

- 64-793 IMMUNOLOGIC RESISTANCE TO THE GROWTH OF BROWN-PEARCE CARCINOMA INDUCED BY INJECTION OF NECROTIC, ELECTROCOAGULATED HOMOLOGOUS TUMOR TISSUE. (E.) Strauss, A. A. (Louis A. Weiss Mem. Hosp., Chicago, Ill.) and M. Appel. Bull. Weiss Mem. Hosp. 5(1):6-17, 1963.

Electrocoagulation of one testicle of a rabbit bearing transplanted Brown-Pearce tumors (BPT) in both testicles caused regression of the tumor in the contralateral testicle. When the normal testicle of a BPT bearing rabbit was electrocoagulated, tumor growth continued unhampered in the contralateral testicle. Similar antibody response was seen with spontaneous mammary tumors in the white rat; electrocoagulation caused either complete regression or growth arrest in 47/64 rats. Those animals in which electrocoagulation produced regression of the primary tumor were completely refractory to the growth of subsequent BPT transplant. If a BPT was electrocoagulated and the necrotic tissue allowed to remain *in situ* at least 7 days before being transplanted, no

tumor grew in the host rabbit; if transplanted on days 2, 3 or 5, the tumors grew. Of 52 rabbits with transplanted coagulated tumors, 32/52 are still alive and well and show no evidence of tumor after 1 yr. despite the presence of viable tumor tissue, and 20/52 died (8 with extensive tumor growth; 5 with no evidence of tumors; 7 with caseous masses). Those with caseous masses were refractory to subsequent tumor transplants. The authors have treated 400 cases of carcinoma of the rectum using electrocoagulation; 5-yr. cures were obtained in 75%, 10-yr. cures in 30%.

- 64-794 LOSS OF TISSUE-SPECIFIC AUTOANTIGEN IN THYROID TUMOURS. A DEMONSTRATION BY IMMUNOFLOURESCENCE. (E.) Goudie, R. B. (Dept. Path., Western Infirm., U. Glasgow, Scotland) and H. M. McCallum. Lancet 2:1035-1038, 1963.

When 22 thyroids were examined by the fluorescent-antibody technic using cytotoxic Hashimoto serum as a specific stain for the cytoplasmic autoantigen, the cells of 4 thyroid carcinomas were deficient in autoantigen and less obvious autoantigen loss was seen in some or all of the cells in 3/6 simple thyroid adenomas and 2/4 adenomatous goiters. Autoantigen loss was slight or absent in normal thyroid and 6/7 thyrotoxic thyroids. These findings may have a bearing on the invasive behavior of thyroid carcinoma cells.

- 64-795 A NEW SPONTANEOUS HAMSTER CARCINOMA ASSOCIATED WITH A POSITIVE ERYTHROAGGLUTINATION REACTION AND ANEMIA. (E.) Sherman, J. D. (Dept. Path., Boston U. Med. Ctr., Mass.), P. G. Rigby, R. L. Hackett and G. H. Friedell. Cancer Res. 23(10):1689-1693, 1963.

A new tumor (MAD 1), probably of salivary origin, discovered in the right anterolateral cervical triangle of an untreated male golden hamster has been serially transplanted in the cheek pouch or flank of normal golden hamsters through 70 generations; the tumor growth curve was stable since the 15th generation and has been 100% transplantable since the 6th generation. Growth of the tumor was associated with the development of a normochromic, normocytic anemia, much like that seen in many human cancer pts. The anemia was not related to blood loss, metastases, cachexia, or infection. The animals develop a positive erythroagglutination reaction, while red cell survival was shortened. The erythrocytes were not intrinsically defective, but an extrinsic destructive mechanism was operative.

- 64-796 SYRIAN HAMSTER TUMOR TRANSFORMATION AFTER 22 MONTHS OF ALTERNATIVE *IN VIVO* AND *IN VITRO* CULTIVATION. (E.) Fadei, L. (Tissue Cult. Lab., Oncol. Inst., Bucharest, Rumania) and M. Nachtigal. Oncologia (Basel) 17(2):89-100, 1964.

Alternate *in vivo* and *in vitro* cultivation

4 times) of Syrian hamster H14 sarcoma (induced by s.c. 20-methylcholanthrene) caused the following modifications: increase in max. tumor area from 4.99 cm² on day 25 (controls) to 28.89 cm² on day 44; local and regional dissemination and patic and contralateral lymph gland metastases; terotransplantability in 20% of mice of generation 34; prolongation of animal survival by 20 days from 30 to 50; increased diameter of the nucleus from 4.83 to 6.94 μ (31st generation); gradually increased mitotic index from 0.15 to 1.29; the appearance of giant cells; increase of the ratio of cells with 57-58 chromosomes and those with 62 chromosomes from 1:1 (generation 18) to 7 (generation 31). The changes were attributed to selection of a differentiated cell type with lower antigens after repeated in vitro cultivation.

797. TRANSMISSIBILITY AND SOME HISTOPATHOLOGY OF A SPONTANEOUSLY ORIGINATED VISCERAL TUMOR IN THE NEWT, TRITURUS PYRRHOGASTER. Inoue, S. (Dept. Anat., Western Reserve U. School of Med., Cleveland, Ohio) and M. Singer. Cancer Res. 23(10):1679-1684, 1963.

A spontaneous tumor of the liver from T. pyrrhogaster was transferred successfully to other urodeles, including T. viridescens, Hynobius lichenatus, and Amblystoma maculatum. The transfer was made by either direct implantation of a piece of fresh tumor into the peritoneal cavity, i.p. inj. of frozen-dried specimens as well as the supernatant of a homogenized and centrifuged sample after repeated freezings and thawings. The tumor was also found in the kidney, gonad, along the intestines. Histologically, the tumor is composed mainly of mononuclear cells and scattered pigmented cells. When the tumor supernatant was inj. into H. lichenatus, 1/5 developed a tumor after 175 days; however, when pieces of liver taken from the newts which did not show tumor development were transplanted i.p. s.c. to 12 T. pyrrhogaster, tumors occurred in 10 of the newts. The supernatant also induced an invasive and destructive growth when inj. into a limb and the growth metastasized to the viscera with small tumors studding the liver, spleen and other parts. Although the nature of the agent of tumor transmission has not been identified, a possible interpretation is that the tumor is caused by a microorganism.

798. CHROMOSOME STUDIES IN ADULT ACUTE LEUKEMIA. (E.) Fitzgerald, P. H. Christchurch Hosp., New Zealand), A. Adams and W. Gunz. J. Nat. Cancer Inst. 32(2):395-417, 1964.

Cell culture studies of 18 adult pts. with acute leukemia showed few chromosomal abnormalities, but abnormal genotypes were found in each of the pts. in whom direct examinations of the bone marrow were made. The abnormalities consisted of both numerical and structural changes that

could not be correlated with any clinical or hematological features and were individual to each case. When the marrow was examined repeatedly in individual pts., the abnormalities persisted regardless of the stage of the disease, though some diminution in their numbers occurred during remission. The findings suggested that the chromosomal abnormalities are intimately associated with, and perhaps an essential part of, the development of acute leukemia.

64-799 SPONTANEOUS TUMOURS IN MICE. (E.) Reddy, D. J. (Upgraded Dept. Path., Andhra Coll. Med., Visakhapatnam, India) and P. S. Rao. J. Indian Med. Prof. 10(2):4805-4807 and 4810, 1964.

Of 1507 mice of both sexes (age and breed not stated), 41 (2.72%) developed spontaneous tumors (37 malignant, 4 benign), all of which were confined to female virgins. Three mice developed multiple tumors. The malignant tumors were of the following type and number: adenocarcinoma of the breast 11; lymphosarcoma and reticulum cell sarcoma 13; hepatoma and angioendotheliosarcoma of the liver 2; fibrosarcoma of the s.c. tissue 2; hydroadenoma, adenoid cystic epithelioma and epithelioma of the skin appendages 3; leiomyosarcoma and endotheliosarcoma of the uterus 2; bronchiolar carcinoma 2; epithelioma of the vagina 1; angioendotheliosarcoma of the omentum 1; adenocarcinoma and granulosa cell carcinoma of the ovary 2.

64-800 ASSOCIATION OF WILMS'S TUMOR WITH ANIRIDIA, HEMIHYPERTROPHY AND OTHER CONGENITAL MALFORMATIONS. (E.) Miller, R. W. (NCI, Bethesda), J. F. Fraumeni, Jr. and M. D. Manning. New Eng. J. Med. 270(18):922-927, 1964.

Among 440 pts. (223 male, 217 female), whose ages varied from <1 yr. to 18 yr., with Wilms's tumor, the following congenital malformations were observed: aniridia 6, hemihypertrophy 3, pigmented nevi 4, internal hemangiomas 4, hemangiomas of the skin 4, hypospadias 5, other urinary tract anomalies 18, cryptorchidism 11, clubfoot 4, etc. The observed incidence of association of Wilms's tumor and aniridia (1:73 cases) was markedly greater than that of the usual rate, 1:50,000. Of 223 boys with Wilms's tumor 11 had cryptorchidism, expected number 3.3; 5 had hypospadias (0.6 cases expected). Thus, Wilms's tumor formation seems to be induced or enhanced by teratogenic influences affecting the genitourinary tract.

64-801 THE SEBACEOUS EPITHELIOMA. A CLINICAL AND HISTOLOGIC STUDY. (E.) Zackheim, H. S. (Dept. Dermatol., Wayne State U., Detroit, Mich.). Arch. Derm. (Chicago) 89(5):711-724, 1964.

The author presents a detailed clinical and histological study of 8 pts., 5 male and 3 female, age 39-75 yr., with 4 additional cases studied but not

described, with sebaceous epithelioma (basal cell epithelioma with sebaceous differentiation). Evidence is presented indicating that they are primary sebaceous gland neoplasms, resulting from the proliferation of the basal (germinative) cells of the gland. A review (33 references) and discussion of the subject is also presented.

- 64-802 FORMATION OF TUMORS CONTAINING BONE AFTER INTRAMUSCULAR INJECTION OF TRANSFORMED HUMAN AMNION CELLS (FL) INTO CORTISONE-TREATED MICE. (E.) Anderson, H. C. (Sloan-Kettering Inst. Cancer Res., New York), P. C. Merker and J. Fogh. Am. J. Path. 44(3):507-519, 1964.

See CRA 1(5):#1005, 1963.

- 64-803 EFFECT OF NEO-NATAL AND ADOPTIVE IMMUNIZATION ON TUMOR TRANSPLANT SUSCEPTIBILITY IN MICE. (E.) Bailey, J. M. (Dept. Biochem., George Washington U. Sch. Med., Washington, D. C.) and K. Merrill. Proc. Soc. Exp. Biol. Med. 115(1):32-39, 1964.

Newborn DBA/2 mice (resistant to CD/5 lymphoma tissue) were cross-immunized (X-imm) by i.p. inj. with 2×10^5 spleen cells obtained from a newborn BALB/C mouse and newborn BALB/C mice (susceptible to CD/5 lymphoma tissue) were X-imm by i.p. inj. with 2×10^5 spleen cells obtained from a newborn DBA/2 mouse. After 6-8 wk. the X-imm and normal mice were inj. s.c. with 10^6 cells of a CD/5 lymphoma cell suspension in the right groin. Tumor susceptibility 11-16 wk. afterward for normal BALB/C, X-imm BALB/C, normal DBA/2 and X-imm DBA/2 mice, resp., was 51/59 (13% immunity), 32/58 (45% immunity), 0/16 (100% immunity) and 3/35 (91% immunity). After an i.p. inj. of 40-80 million lymph and spleen cells (20% from lymph nodes and 80% from spleen obtained from one of the tumor-resistant normal DBA/2 mice), 7/29 X-imm BALB/C mice showed complete regression within 1-2 wk. with no reappearance of a tumor in 3 mo., 8/29 showed partial tumor regression and 14/29 did not respond, except for the appearance of necrotic tissue in 10/14. The same treatment produced no tumor regression in 12 normal BALB/C mice; but 1 showed a slower tumor growth rate and 3 had necrotic tissue. This resistance to tumor development was not associated with an ability to develop a precipitin titer against tumor protein.

- 64-804 HISTOLOGY OF SOME NEOPLASMS AND NON-NEOPLASTIC LESIONS FOUND IN WILD MICE MAINTAINED UNDER LABORATORY CONDITIONS. (E.) Dunn, T. B. (NCI, Bethesda) and H. B. Andervont. J. Nat. Cancer Inst. 31(4):873-901, 1963.

A variety of spontaneous tumors occurred in a colony of wild house mice (*Mus musculus*) kept in captivity for 10 yr.: 26 reticular neoplasms (RN; 1 Type A, 2 lymphocytic leukemia and 23 Type B); 1 teratoid tumor on the side of face of a 10-week-old mouse (TT); 9 ovarian granulosa cell tumors (OT; 2/9 contained several different cell patterns); 1 tumor from the foot pad (FPT; composed chiefly of acanthomatous tissue); 1 osteogenic sarcoma (OS); and 1 visible mast cell neoplasm (MN) in the stomach wall. Histological comparisons with tumors of inbred mice showed that TT, OS, OT and FPT were similar in both types and occurred only by induction in inbred mice). The following differences characterized the tumors of inbred mice: lack of variety of cell patterns in OT; general microscopic size of MN; high incidence of lymphocytic leukemia, rather than Type B, in RN. A high incidence of lymphocytic leukemia occurred in the wild mice only when Moloney virus was admin. The diversity of tumors occurring spontaneously in the wild mice colony was much greater than in inbred mice.

- 64-805 KARYOTYPIC AND MORPHOLOGIC CHARACTERIZATION OF A SERIALY TRANSPLANTED HUMAN CHORIOCARCINOMA. (E.) Galton, M. (Dept. Path., Dartmouth Sch. Med., Hanover, N. H.), P. B. Goldman and S. F. Holt. J. Nat. Cancer Inst. 31(4):1019-1035, 1963.

A human choriocarcinoma, derived from a cerebral metastasis and adapted to serial passage in the wall of the cheek pouch of a golden hamster (*Mesocricetus auratus*) retained the same morphology after 1 yr., but displayed an irregular aneuploid karyotype (modal value of 80 at generation 56, rising to 88-92 in 9 mo. at generation 80). A slightly enhanced tumor growth and an increase in the proportion of syncytiotrophoblast was seen after admin. of dehydroisoandrosterone acetate (15 mg in suspension of propylene glycol i.p. or s.c.). The following factors indicate that the passages were descendants of the cells originally derived from humans: chromosome distribution was morphologically similar; satellites on acrocentric chromosomes were like those of human cells; the increase in the number of small chromosomes was proportional to the ploidy; and the sensitivity to colchicine was like that of human cells.

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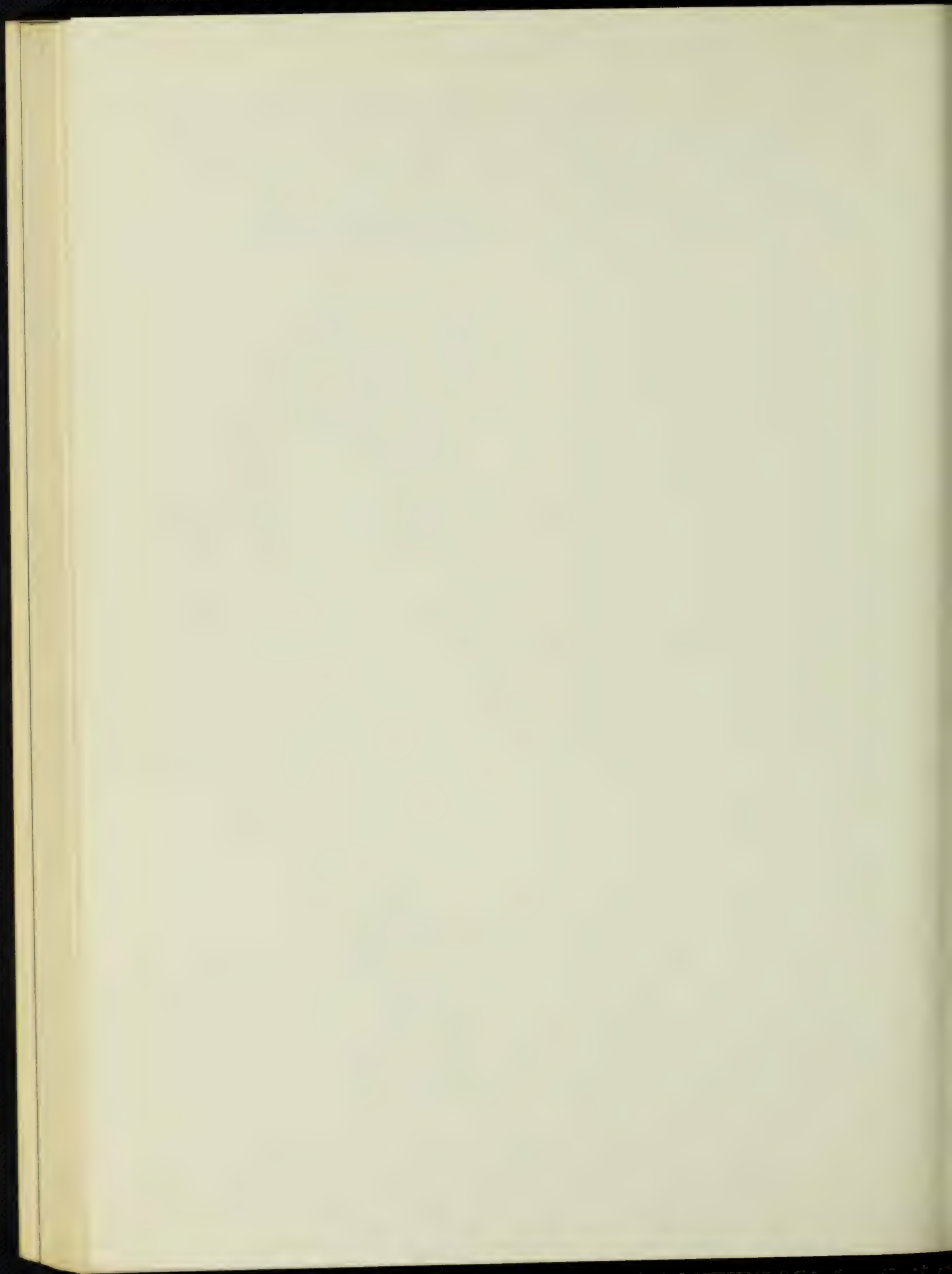
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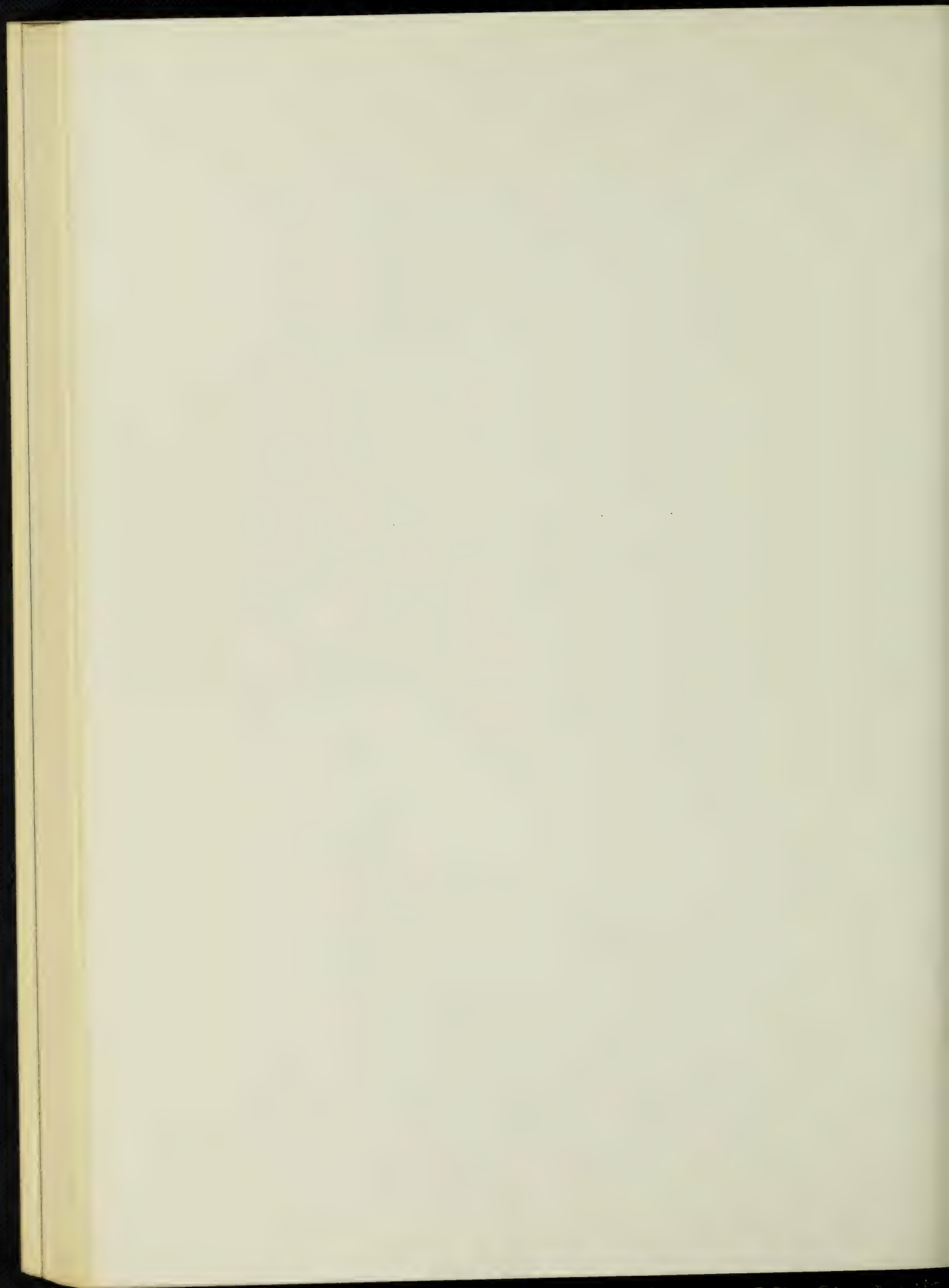
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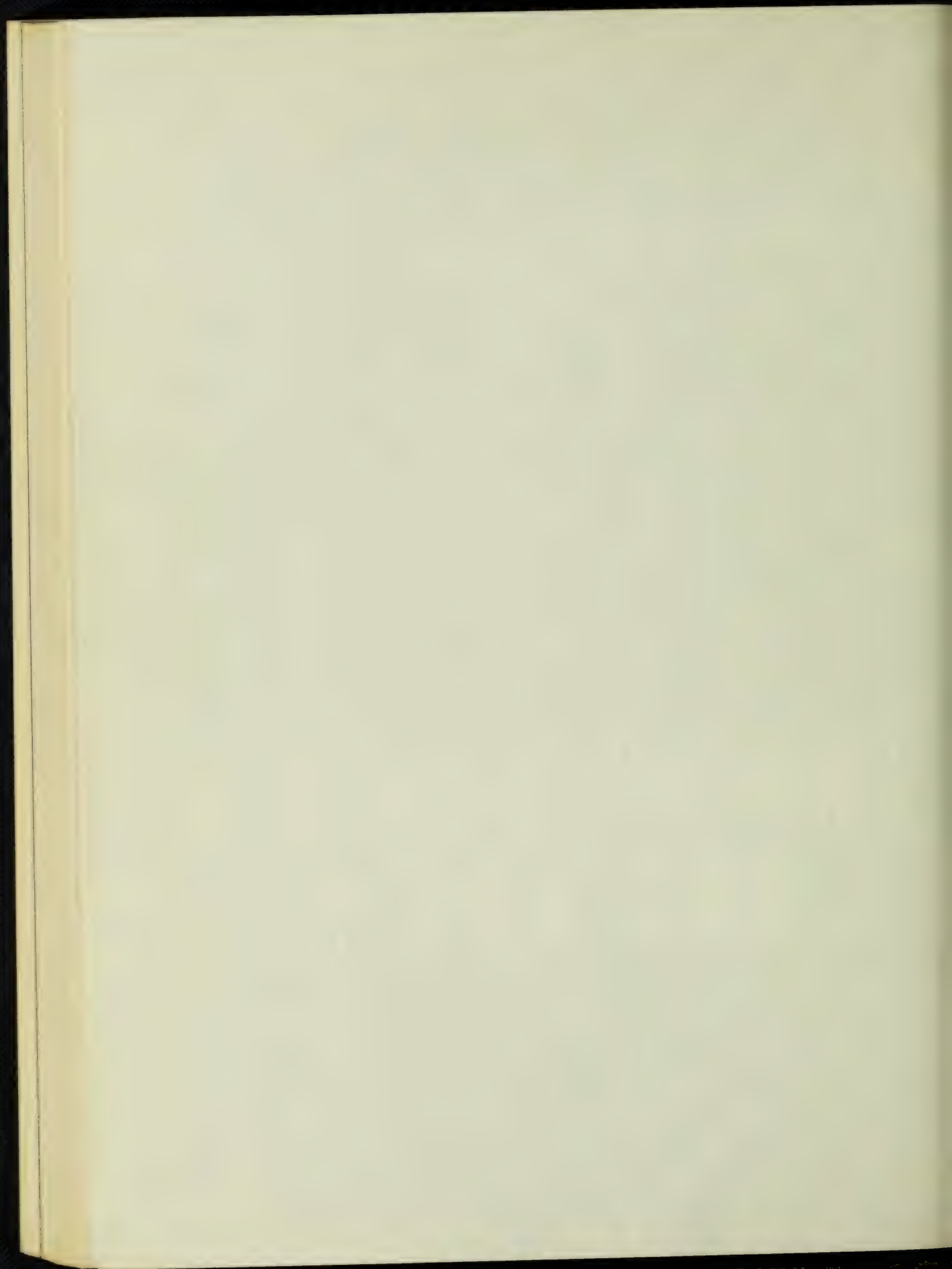


CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS

ABSTRACTS

Volume 2, Number 5
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum, maximal
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubate(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

806 GEOGRAPHIC ASPECTS OF MALIGNANT DISEASE. (E.) Phillips, A. J. (Natl. Cancer Inst. Canada, Toronto). Canad. Med. Assn. J. 19:1095-1098, 1964.

A review of some geographic differences in the epidemiology of various malignant diseases, very high incidence of primary cancer of the liver (35% of 7,500 cancer cases) was seen in that part of Africa south of the Sahara Desert, while this malignancy accounts for only 160-24,000 (about 0.75%) cancer deaths per yr. in Canada. The association of chronic malnutrition and cirrhosis (kwashiorkor) is an important tributary cause. In the past 8 yr., 106 children with malignant lymphoma (av. age of 6.5 yr.) have been seen in central Africa, as compared to 41 cases in 30 yr. seen at New York's Memorial Hospital. High incidences of cancer of the stomach have been seen in Japan and Chile; in Iceland this has been 45% of all male and 31% of all female cancer deaths. Deaths from stomach cancer, however, in U.S. Japanese males and Hawaiian Japanese were 90% and 72% lower, resp. In Canada, since 1940, there has been a decline in the death rate (per 100,000) from stomach cancer: from 17 to 21.6 in males and from 18.1 to 10.9 in females. Betel-chewing and inverted cigar smoking have been related to oral cancer incidence in India; cancer of the skin of the lower abdomen and thigh in Kashmir is attributed to carrying kettles filled with smoldering dry maple leaves over the clothes. Cancer of the skin, of which the highest incidence is found in Australia, seems to increase as latitude decreases. (9 references)

807 THE RODENT LEUKEMIAS: VIRUS-INDUCED MURINE LEUKEMIAS. (E.) Moloney, J. B. (NIH, Bethesda). Ann. Rev. Med. 15:383-392, 1964.

For listing the murine leukemia viruses, the author reviews the pathology and pathogenesis of leukemias induced by these viruses, their structure and site of multiplication. The experimental transmission of the leukemia agents to mice and rats (see CRA 1(1):#113, 1963) and the role of nucleic acids in the biological activity of the viruses are discussed. Some of the biological and immunological studies on the relationships of the leukemic viruses are reviewed. (80 references)

808 ATMOSPHERE POLLUTANTS. (E.) Kotin, P. (NCI, Bethesda) and H. L. Falk. Ann. Med. 15:233-254, 1964.

Assessment of the effects upon humans of atmospheric chemical pollutants is made in terms of source of emission, photochemical and photolytic reactions, and meteorologic and climatic factors. Acute hazardous episodes from polluted air (PUA) are presented from Belgium,

Mexico, USA and England as well as effects from chronic exposure as in Los Angeles, Tokyo and New Orleans. The following known components of PUA were analyzed according to physical and chemical properties with the intention of defining their mechanism of pathological effect: aerosols, gases, sulfuric acid, organic peroxides, formaldehyde, acrolein, ozone, sulfur dioxide, oxides of nitrogen and their products, carbon monoxide, fluorides, lead, beryllium, soot, polycyclic aromatic hydrocarbons and products of aliphatic hydrocarbons. Persons with antecedent chronic cardio-respiratory diseases and those in the extremes of age are unusually susceptible to health hazards from PUA. (See also CRA 1(8):#1426, 1963; and ibid., 2(2):#171, 1964.) (109 references)

64-809 IMMUNOLOGICAL FACTORS IN THE PROCESS OF CARCINOGENESIS. (E.) Burnet, M. (Walter-Eliza Hall Inst. Med. Res., Melbourne, Australia). Brit. Med. Bull. 20(2):154-158, 1964.

Cell surveillance whose evolutionary function is to prevent the emergence of malignant mutant cells is described as the parent concept of homograft immunity. Somatic mutations produce well marked surface characteristics by which they can be differentiated. Carcinogenesis is viewed as a wide range of independent or sequential somatic mutants which survived these local selective pressures, allowing malignancy to emerge. Viruses can repeatedly induce a single specific change in cell histocompatibility antigens: these are also genetically labile. A positive role of immune processes in the production of malignant disease is not implied, but they are important in determining the character of the tumor. (48 references)

64-810 EFFECTS OF CARCINOGENS ON IMMUNE PROCESSES. (E.) Berenbaum, M. C. (St. Mary's Hosp. Sch. Med., London). Brit. Med. Bull. 20(2):159-164, 1964.

The carcinogens shown to inhibit immune responses are radiation, alkylating agents, polycyclic hydrocarbons and urethan. They generally lengthen the induction period, reduce the initial rate of immunity increase and the max. level of reactivity and its duration. This correlation between carcinogenicity and immunity inhibition is only partial. This inhibition has its greatest effect on primary antibody response and first-set homograft reaction. Antibody production is more readily inhibited than is induction of delayed hypersensitivity or homograft rejection. Different techniques and quantity of antigen make these comparisons inconclusive. Inhibition is also highly dependent on the time of admin. of antigen and inhibitor. Other possible mechanisms of action discussed are: toxicity, inhibition of antigen uptake or disposal, lympholysis and differential general sensitivity of immunological cells. (126 references)

- 64-811 SEX HORMONES AND CARCINOMA OF THE LARYNX. (Ger.) Loewit, K. Mschr. Ohrenheilk. 97(10):436-439, 1963.

In a review of the probable relationship between cancers of the larynx and disturbances of sexual hormonal function, it is indicated that approx. 95% of the pts. developing such cancers are males; that they are commonly associated with an androgen deficiency; and that no case has ever been reported as occurring in a hypogonadal male, a congenital eunuch, an early castrate, or a pt. with prostatic cancer. In the first case ever reported as occurring in a pt. with Klinefelter's syndrome, a 32-year-old, married male without issue showed normal levels of testicular androgen production despite typical Klinefelter's symptomatology in other respects. Indicated as a possible contributory factor to tumor development was a history of smoking since age 20, and of heavy smoking during the 3 yr. preceding diagnosis. (29 references)

- 64-812 CARCINOGENIC ADENOVIRUSES. (Fr.) Thomas, M. (Res. Inst. Leukemia, Saint-Louis Hosp., Paris). Path. Biol. 12(5-6): 330-334, 1964.

A general review on carcinogenic adenoviruses taken mostly from the experimental data of J. J. Trentin et al. and R. J. Huebner et al. (See also CRA 1(3):#465; ibid., 1(5):#900, 1963; and ibid., 1(9-10):#1740, 1964.) (20 references)

- 64-813 PRESENT KNOWLEDGE OF THE ASSOCIATION OF BLOOD GROUPS AND DISEASES WITH SPECIAL REFERENCE TO THE STUDIES ON GASTRIC CANCER IN U.S.A. AND JAPAN. (E.) Desai, R. G. (Massachusetts Mem. Hosp., Boston U. Med. Ctr.) and W. P. Creger. Bibl. Haemat. (19):709-718, 1964.

This review of approx. 35,000 gastric cancer pts. with known blood groups from 23 different countries, shows the mean relative incidence of blood groups A:0 to be 1.22 ($p < 0.001$). Comparison of red cell antigen incidence in USA white and Japanese gastric cancer pts. showed the following, resp.: Group 0, 44.8% (controls 47.2%) and 29.65% (controls 30.6%); for Group A, 36.2% (controls 38.17%) and 34.75% (controls 38.3%); for Group B, 12.4% (controls 10.6%) and 24.5% (controls 21.7%); for Group AB, 6.7% (controls 4.1%) and 11.10% (controls 9.4%). Rh, MN, Kell and Duffy antigen systems have also been studied in the two ethnic groups. (See also CRA 2(4):#748, 1964.) (64 references)

- 64-814 ENDOCRINE ASPECTS OF ENDOMETRIAL CARCINOMA. (Sp.) Lienhard, C. P. (Dept. Gynec., U. Buenos Aires Sch. Med., Argentina). Orientac. Med. 13(594):18-20, 1964.

A review of conflicting reports concerning the

incidence of uterine endometrial carcinoma in association with Stein-Leventhal's syndrome, functioning estrogenic ovarian tumors and other endocrine or metabolic disturbances. Note is also made of conflicting reports concerning "protection" afforded by bilateral ovariectomy. The author concludes that too little is known concerning the mechanisms involved in the development of this type of tumor to permit drawing any conclusions with respect to the possible role of hormonal influences on the one hand and endometrial hyperplasia due to non-hormonal causes on the other. (34 references)

- 64-815 TUMEFACTION IN PLANTS: ITS RELATIONSHIP TO THE PROBLEM OF CANCER. (Fr.) Gautheret, R.-J. Ann. Pharm. Franc. 22(2): 147-158, 1964.

A review of similarities in the process of tumefaction as seen in plants and in animals. Parallels are drawn between carcinogenesis in animals and tumor induction in plants. In both, transplantability is a criterion of malignant transformation. In both kingdoms, carcinogens include hydrocarbons, viruses, and hormones. In both, hormonal imbalance (auxin/kinin ratio in plants, estradiol balance in man) and development of hormone-independent tumors are comparable: injury and wound healing provide additional stimuli. Genetic carcinogenesis, in plants, is exemplified by tumor formation in the tobacco hybrid *Nicotiana glauca* x *N. Langsdorfii*. In crown gall of plants, induced by *Agrobacterium tumefaciens*, carcinogenesis requires a biologic factor (the bacterium) plus a chemical factor (auxin), just as in the Shope rabbit papilloma both a virus and a carcinogenic carbide are required for malignant tumor production. It is suggested that in crown gall the carcinogen may be, not the bacterium but an associated virus which it carries. Various theories of carcinogenesis in crown gall are outlined. The author concludes that the relatively simple reactions of plants, together with their ability to proliferate in a wide range of synthetic media, make it possible to use them to study problems of carcinogenesis which are not as yet accessible to study in animal cells. (See also CRA 1(12): #2227; and ibid., #2237, 1964.) (No references)

- 64-816 VIRUSES AND BLOOD DISEASES. (Fr.) Derray, J.-M. Vie Med. 45:287-308, 1964.

A review is presented citing viral intervention in both benign and malignant hemopathies, with the intention of delineating a viral etiology. Under the first classification the following were discussed: infectious mononucleosis, benign lymphoreticulosis of the cat's claw, acute infectious lymphocytosis and other known viral affections. Under the second classification (which was treated more thoroughly), the following were discussed: Rous sarcoma, avian leukoses, mammalian leukemias and, finally, a presentation of the current

dence of viral etiology for human blood diseases; Burkitt's tumors, Hodgkin's disease and leukosis present the best evidence of possible viral etiology. (No references)

817 VIRUSES, CHROMOSOMES AND LEUKEMIAS. (Fr.) Lépine, L. and C. E. Ford. *Cours Med.* 85(44):5893-5896, 1963.

A brief review considers such factors as chromosomal influence, irradiation treatment, species differences, changes of viral DNA and RNA, chromosomal modifications (with associated blood group dispositions) and transplant susceptibility. In discussing the possible interrelationship between viruses, chromosomes and leukemias. In conclusion, the virus is viewed as the initiator which induces the chromosomal anomalies which, in turn, will lead to the selection and proliferation of an abnormal clone which is the cancer itself. (No references)

818 SARCOMA OF THE SOFT TISSUES AND TRAUMA IN EXPERT TESTIMONY ON ACCIDENT CASES. (r.) Betzler, H. J. (Surg. Clin., U. Tübingen, Germany). *Vorträge aus der Praktischen Chirurgie*, 67. Ferdinand Enke (Publ.), Stuttgart, 1964.

An extensive review of the incidence, latency and anamnestic background of sarcomas of the soft tissues arising after documented trauma at the wound site, the author concludes that a genuine traumatic etiology is extremely rare and continues to be problematic in many cases which have been reported as "verified". When sarcomas arise within a yr. following an accident (particularly, following direct or indirect trauma due to a sharp instrument or of such nature as to leave an "encapsulated" area of tissue damage), activation of a latent tumor must be assumed in most cases, probably via occult bleeding into the wound or tumor-bed and consequent disturbance of tissue function and metabolism. The average latency period for the appearance of sarcomas following such injuries is 16 mo.; following open wounds or other "open" injuries, 13 yr.; following wounds due to firearms, 12 yr.; following irradiation trauma, 21 yr. Thus today (in contrast to earlier practice), the presence of a long latency period in conjunction with demonstrable scarring or other continuing source of secondary trauma is considered positive evidence in favor of a causal relationship between the initial trauma and subsequent tumor development. The author also emphasizes the importance of comitogenic factors in sarcomas arising out of scar tissue, pointing out that the nature of the wound, as well as its extent and severity, is of critical importance from the point of view of carcinogenesis. (128 references)

819 ANIMAL LEUKOSES (LEUKEMIAS). (Ger.) Wirth, D. Pp. 101-115 in *Handbuch*

der Gesamten Hämatologie (Handbook of General Hematology) Vol. 4. Special Hematology. Pt. 2. Heilmeyer, H. C. L. and A. Hittmair (Eds.). Urban and Schwarzenberg (Publ.) Munich. 693 pp., 1963.

A general review details the differences between leukemias arising in man and in various species of animals, as well as the differences observed between the species discussed. Included are sections on dogs, cats, swine, horses, sheep and goats, guinea pigs, white mice, cattle and domestic fowl. Report is also made of the discovery of leukemias or leukemic-like disorders in 17 species of wild animals and 15 species of birds. The possible etiologic roles of chemical carcinogens, trauma, exposure to radiation and viruses are discussed briefly and treatment measures are summarized for some types of animal. The author concludes that present knowledge does not permit a conclusion as to whether or not leukemias in man are actually the same disorders as their apparent counterparts in animals; it seems possible that 1 or more common (or similar) etiologic factors may be involved, with differences in the actually presenting disorders resulting from species-specific morphologic and/or biologic characteristics. (38 references)

64-820 INDUCTION OF EXPERIMENTAL LEUKEMIAS BY MEANS OF VIRUSES. (Ger.) Graffi, A. Pp. 90-101 in *Handbuch der Gesamten Hämatologie (Handbook of General Hematology)* Vol. 4. Special Hematology. Pt. 2. Heilmeyer, H. C. L. and A. Hittmair (Eds.). Urban and Schwarzenberg (Publ.) Munich. 693 pp., 1963.

In a detailed review of experimentally induced leukemias of viral origin in fowl and mice, the author reviews attempts to induce experimental leukemias or related disorders (particularly, in mice) by inoc. of blood, cerebral filtrates, splenic or lymph node fractions or filtrates, et al, derived from leukemic pts. Although successful takes have been relatively few and erratic, the author points out that the heterologous nature of hosts and donors, as well as their relatively distant phylogenetic relationship, tends to militate against even this degree of success. He suggests that results achieved to date may have considerable potential significance, even though they can not, as yet, be interpreted as a definitive confirmation of the viral etiology of these disorders. (94 references)

64-821 ARSENIC AND LUNG CANCER. (E.) Editorial *Brit. Med. J.* 1(2):1656, 1964.

A review article considers the correlation between arsenic and lung cancer. The inevitable question, does arsenic play any part in causing lung cancer among cigarette smokers? is asked. Many pertinent findings, including one that notes 12.5 µg of arsenic as the daily dose from smoking in the peak period of arsenical insecticides, led committees

reporting to both the Surgeon General of the U.S. Public Health Service and to the Royal College of Physicians to reject arsenic as a factor of prime importance in the genesis of cigarette smokers' cancer. Exposure to arsenic, the article concludes, by air pollution or cigarette smoke, is difficult to regard as having anything more than a small adjuvant role in the incidence of lung cancer. (13 references)

- 64-822 GENITAL HORMONES AND CANCER. (Fr.) Dargent, M. (Dept. Med., U. Lyon, France). Lyon Chir. 59(6):915-928, 1963.

In a discussion on hormone dependence and cancer, the author reviews some of the current biologic and therapeutic data on cancer of the prostate, breast and endometrium. Hormonal influence in breast cancer varies: response is most frequent in women at age 45 (premenopausal period) and 65 (postmenopausal period) and in men at the age of 55 and 75; high frequency of chronic alcoholism and cirrhosis in the etiology of male breast cancer, indicating defective steroid transformation in the liver; same incidence (1-1.5%) in both men and castrated females; rarity during periods of increased estrogen activity. Endometrial cancer is usually seen in older women after cessation of ovarian activity and frequently appears in association with obesity, diabetes mellitus and hypertension. Held reports 246/376 cases (64.4%) in which endometrial cancer appears in combination with one or all three of the above mentioned conditions. (No references)

- 64-823 A REVIEW OF THE CHEMICAL INDUCTION OF NEOPLASMS IN AMPHIBIA. (E.) Balls, M. (Dept. Exptl. Zool., U. Geneva, Switzerland) and L. N. Ruben. Experientia 20(5):241-247, 1964.

A review is presented of 41 papers in which attempts were made to induce tumors in Anura (14 reports) or Urodela (27 reports) amphibians, chiefly with methylcholanthrene, benzpyrene and dibenzanthracene. Epidermal hyperplasia was noted in 2 and 15 reports, resp. A total of only 9 malignant tumors was noted: 1 adenocarcinoma, 1 carcinoma, 4 lymphosarcomas, 2 spindle cell sarcomas and 1 sarcoma. The 4 lymphosarcomas and 1/2 spindle cell sarcoma were transplantable. The renal adenocarcinoma in *Rana pipiens* and the 3 lymphosarcomas in *Xenopus laevis* represent augmentation of incidence of normally expected tumors while the others would represent *de novo* induction (1 sarcoma in a *R. pipiens* tadpole, 1 each spindle cell sarcoma in *Siredon mexicana* and *Triturus viridescens*, a lymphosarcoma in *T. cristatus* and a carcinoma in *T. alpestris*). The author also discussed carcinogenic studies in relationship with regeneration and embryonic development as a positive argument for using this class as a means of study. (See CRA 2(3):#509, 1964.) (65 references)

- 64-824 EVALUATION OF THE TERATOGENICITY OF DRUGS. (E.) Cahen, R. L. (Lafon Res. Ctr., Maisons-Alfort, France). Clin. Pharmacol. Ther. 5(4):480-514, 1964.

The author reviews the following therapeutic compounds: thalidomide, antimetabolites (6-mercaptopurine, azaserine, 6-chloropurine), nitrogen mustard, urethan, steroids and hormones, and hypoglycemic agents, and presents the difficulties that have prevented a systematic and complete evaluation of their teratogenic effect. Compounds proven to be teratogenic only in experimental animals are also discussed; these demonstrate a great range in sensitivity and species differences. There was no obvious relationship between chemical structure and teratogenic effect, as the latter presents a similar spectrum of embryopathies despite the marked variation in structure of the many compounds. The numerous aspects involved in detecting, screening and evaluating teratogenic drugs are then discussed at length. (See also CRA 2(5):#879, 1964.) (262 references)

- 64-825 RECENT STUDIES IN AUTOIMMUNITY. (E.) Dameshek, W. (Pratt Clin., New England Ctr. Hosp., Boston, Mass.). Acta Haemat. 31(4):187-199, 1964.

After reviewing the advances made in the last few years in the study of autoimmune disorders, the author views this condition as a consequence of clones of abnormal immunocompetent cells which, failing to recognize normal cell antigens, produce autoantibodies. In the presentation of this concept, other subjects discussed are the immunocompetent cell, immunocyte proliferation and its relationship to leukemia, the thymus as the important primordial site for lymphoid and immunologic competence, the graft vs. host phenomenon with particular reference to lymphoproliferative disorders and systemic lupus, the abnormal clone and the state of broken tolerance. (42 references)

- 64-826 LEUKEMIA FOLLOWING IRRADIATION. (E.) Gunz, F. W. (Dept. Path., Christchurch Hosp., New Zealand) and H. R. Atkinson. Radiology 82(6):1067-1071, 1964.

Several surveys which have cited radiation-induced leukemia are reviewed in this editorial presentation and are used to approximate a dose-response curve as well as the probable incidence of this type of leukemia. Present evidence indicates a linear response curve of 1-2 cases/rad/yr./1 million persons exposed to marrow doses in excess of 50-100 rad. Below this range, the shape of the curve remains unknown. Calculations from these surveys also indicate that in the U.S. 4.8% of childhood (under 15 yr.) leukemia may have been radiation-induced, and that with adults not more than one third of 1% of all leukemias could be caused by diagnostic radiation. The total number of conclusive cases of radiation-induced

ukemia is estimated to be well below 500.
See also CRA 2(3):#443, 1964.) (32 references)

- 827 CARCINOMA OF THE BLADDER. (E.)
Wallace, D. M. J. Roy. Coll. Surg.
inb. 9(2):107-114, 1964.

In this broad review there is a brief consideration of experimental and industrial carcinogenesis. About 1% of all bladder tumors seen each yr. are due to industrial exposure to β - or α -naphthylamine, benzidine, or to either of 2 azo dyes--auramine or magenta. While β -naphthylamine has not been made in Great Britain since 1950, tumors induced by it still turn up in workers in the dye and chemical industries. Benzidine and α -naphthylamine (containing up to 5% β -naphthylamine as an impurity) are still made. The 2 dyes are used in the clothing trade but are also used in cardboard and in gaudily colored children's comic papers. There is no other cancer where the industrial tumor resembles both the experimental and the spontaneous tumor. Experimental studies in dogs and the metabolism of β -naphthylamine (and its impact on therapy) are also discussed. (No references)

- 828 CONSEQUENCES OF PRENATAL RADIOGRAPHY.
(E.) Editorial. Lancet 1:1204, 1964.

In a discussion of the possible risk of leukemia due to prenatal radiography, it is stressed that quantitative data is needed as to dose, time of pregnancy and possible duration in time. It is noted that all published surveys (11 to date) did not differ significantly as to the increased risk--the best estimate puts this at 40%. The question of dose is complicated by changes in X-ray technic; furthermore, with each passing year, there is less and less chance of salvaging necessary information concerning pts. exposed to out-dated X-ray technics. (5 references)

- 829 MORE CALCIUM AND CANCER. (E.)
Editorial. Lancet 1:1204-1205, 1964.

Criticism is presented of the idea of A. Elkeles that tissues with an increased affinity for calcium enjoy relative immunity from malignant change based on the observation of reduced calcification

of the abdominal aorta in cancer pts.). A second paper by Elkeles would appear to refute this idea; however, the author indicates the growths in the latter group were of an unusually low degree of malignancy. Despite gaps in the data and in the composition of control groups, the idea remains attractive. Cited are works that show low or no calcium content in cancer tissues; inability of fulminating growths to take up calcium from the blood; and the role of calcium lack at the cell surface in relation to adhesiveness, and, perhaps, in relation to some of the disorganized behavior of malignant cells. (7 references)

- 64-830 THE PROBLEM OF THE BENIGN HYPERPLASIOGENOUS AND AUTONOMOUS MALIGNANT BLASTOMA.
(E., Abstract) Rotter, W. Excerpta Med. (Int. Congr. Ser.) (79):E2, 1964.

The author discusses several factors which distinguish benign and malignant tumors. Benign tumors, or hyperplasiogenous growths, occur generally as a result of excessive or disturbed hormonal, humoral or neural adjustment. The response of the cells is partially predetermined by the genotype, yet there is little loss of cell differentiation. In the author's opinion, these cells differ from those of malignant tumors by their unconditional dependence on the stimulating agents. Malignant tumors grow autonomously; the growth is possibly facilitated by some genetic change or predisposition. It is these undetectable predisposed cells that are affected by carcinogens. Only the few cases of human viral malignancy give evidence of a direct causative carcinogen. The intermediary position between benign and malignant tumors of basal cell tumors is discussed, as well as other comparative histologic factors. (No references)

- 64-831 ANTI-TUMOR AGENTS, III. (Jap.)
Osato, S. (Cent. Hosp., Akita Pref., Japan). Shindan to Chiryō (Diag. Ther.) 52(1): 150-159, 1964.

In this paper the author reviews the metabolism of carcinogenic agents such as aminoazo dyes and their effects on cell ultrastructure and on the biochemical changes in liver cells. (28 references)

See also abstract nos.: 879,1004

PHYSICAL CARCINOGENESIS

- 64-832 THE REACTION OF THE ORGANISM TO ACRYLIC IMPLANTS AND THEIR CARCINOGENIC EFFECT IN ALLOPLASTY. (Cz.) Barvic, M. (Dept. Biol., Charles U., Prague, Czech.). *Acta Univ. Carol. (Med.) (Praha)* 8(8):707-750, 1962.

As a part of a systematic investigation of the biological properties of plastics used in dentistry, surgery, and ophthalmology, the author has studied chiefly polymethacrylates or mixtures of their copolymers. The hard or soft resins, when implanted s.c. or i.p. into rats or rabbits, caused only foreign body reactions, i.e., inflammation and the formation of a connective tissue capsule around them. Hydrocolloidal neutral or alkaline, transparent, methacrylates and a white milky specimen #303 (no defined formula) produced various degrees of irritation despite the similarity of their chemical formulas; #303 was tolerated best. The commercial preparations were more inflammatory than their analogs prepared in the laboratory, thus suggesting that pure hydrocolloid methacrylates are non-irritating. Solid acrylic implants resulted in 30 tumors in 450 rats during a period of 3 yr.; 7/30 were spontaneous and appeared in various locations. Four (2 benign, 2 malignant) were probably induced and 19 (1 benign, 18 malignant) were definitely induced. Among the induced tumors, 10/19 were sarcomas resembling Walker 256; 9/19 were carcinomas. Only solid plates (in contrast to perforated plates) led to neoplastic changes; the larger the plate, the greater was the reaction and the shorter the latent period. No case of tumor formation due to acrylics used in alloplasty has been so far reported for humans.

- 64-833 AMINO ACID SYNTHESIS IN CONNECTIVE TISSUE CAPSULES DURING CARCINOGENESIS INDUCED BY PLASTIC IMPLANTS. (Rus.) Berezov, T. T. (Dept. Biochem., Patrice Lumumba U., First State Med. Sch., Moscow) and A. Kh. Kogan. *Biokhimiya* 29(2):218-222, 1964.

White male rats with implanted plastic capsules around the kidney were sacrificed at various stages of carcinogenesis; observations were made from 30 days to 9.5 mo. or longer. The decrease of alanine-transaminase activity was well marked and that of aspartate-transaminase somewhat less pronounced in the process of carcinogenesis. Synthesis of amino acids by reduction was smaller than by reamination, being in normal connective tissue 10-22 times and in tumor 4.9-18 times smaller. In the process of carcinogenesis marked decrease in the reduction amination of the most tested α -keto acids was observed. In the preparations studied, asparagine-transaminase was absent, and glutamine-transaminase was present in traces or absent. In the presarcomatous and sarcomatous tissue and normal connective tissue, active glutaminase I and less active asparaginase I were found.

- 64-834 TUMOR INDUCTION WITH ASTATINE-211 IN RATS: CHARACTERIZATION OF PITUITARY TUMORS. (E.) Yokoro, K. (Dept. Path., Francis Delafield Hosp., Columbia U., New York), A. Kunii, J. Furth and P. W. Durbin. *Cancer Res.* 24(4): 683-688, 1964.

Astatine (At^{211}) inj. i.p. (0.3 μ C/g) induced pituitary tumors (PT) by approx. 25 mo. in 64.7% of male and 55% of female W/Fu rats which had been on a low iodine diet for 6 days previously. All thyroid glands were completely destroyed and atrophy occurred in the gonads. Of the 11 female PT-bearers, 72.7% also had mammary tumors (MT) and all mammary glands were hyperplastic; 45.5% had tumors of another endocrine organ. Among 11 males with pituitary tumors 9.1% had mammary tumors and 45.5% had another endocrine tumor. Four successfully transplanted PT were found to be mammo-somatotropic; the fifth is still under study.

- 64-835 EFFECT OF PROTON TUNNELLING IN DNA ON GENETIC INFORMATION AND PROBLEMS OF MUTATIONS, AGING, AND TUMORS. (E.) Lowdin, P.-O. (U. Florida, Gainesville). Pp. 161-181 in *Biopolymers. Quantum Aspects of Polypeptides and Polynucleotides*. Sym. 1. Stanford U., Cal. March 25-29, 1963. Weissbluth, M. (Ed.). Interscience Publ. Easton, Pa., 565 pp., 1964.

By applying laws of modern quantum theory to the now classic Watson-Crick's model of DNA, the author offers an explanation of how the genetic code might be altered through proton exchange, thus giving rise to mutations. Furthermore, during the replication of DNA, when protons must take sides, traversing a distance of 0.1 μ , there is a time-dependent process which might lead to a loss of genetic information through proton leakage. The cell would then lose the ability to synthesize some of the enzymes necessary for metabolism. Thus, proton-tunneling might be a primary factor in aging and somatic mutations which may give rise to spontaneous tumors and cancer.

- 64-836 X-RAY SENSITIVITY OF SARCOMAS. (E.) Pick, E. (Hebrew U.-Hadassah Sch. Med., Jerusalem). *Lancet* 1:833, 1964.

After discussing the findings of R. P. Pugh et al. that ionizing radiations could induce formation of new antigens in cells, thereby enhancing immunologic rejection of these artificial body-alien components, the author suggests that, similarly, an *in vitro* irradiated tumor autograft could provide a strong, modified antigenic stimulus in an otherwise tumor-tolerant organism. Those tumor cells still viable after irradiation of the original tumor are likely to have their antigenicity modified in a manner similar to that of irradiated autografts, making the remaining 10% of the tumor the ideal and

specific target for an immune response elicited by the autograft. This can be a possible explanation for delayed tumor growth.

4-837 ASBESTOS AS A POTENTIAL CARCINOGEN FOR FOWLS. (E., Abstract) Peacock, A. and P. R. Peacock. Pp. 534-535 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

3 groups of White Leghorn fowls (both sexes), inj. once or twice in the axillary air sacs with asbestos or asbestos-like compounds, 30 survived for periods of a yr. or more and were examined postmortem for possible lesions or tumors. Two tumors, apparently attributable to the asbestos, were described. One, a mucus-secreting adenocarcinoma (observed about 1 yr. after inj. of laboratory grade asbestos) involving the syrinx, the proventriculus, lungs and ovary, might have originated in any of these organs but probably in the respiratory or digestive tract. The second (noted 3 yr. after inj. of a sample of crocidolite suspended in tributyrin) was a large firm tumor, extending along the left air sac (site of inj.) into the humerus, thorax and left lung, which had the appearance of a reticulosarcoma. The authors feel that the presumption, that asbestos is a slow acting carcinogen for the respiratory tract of fowls as it is for man, is justifiable.

4-838 BONE MARROW THERAPY AFTER LEUKAEMOGENIC IRRADIATION. (E., Abstract) Wallis, V. and P. C. Koller. Pp. 115-116 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Mice (C57Bl x CBA/T6T6)F₁, having one minute marker chromosome, were given 4 weekly doses of 10 r X-rays starting when 30 days old and i.v. inj. of 3×10^7 bone marrow cells of CBA/T6T6 with two T6 markers or BALB/c cells with no chromosome markers, within $1\frac{1}{2}$ hrs. after irradiation. The mice, killed 30, 70, and 120 days later, had their dividing cells scored as host or donor type depending on the number of T6 chromosomes present. No dividing cells were found after 30 or 70 days in the mice given CBA/T6T6 cells, but in the mice killed at 120 days, 3% of the dividing cells were of the host type; in the mice given allogeneic bone marrow,

all dividing cells were host type. Cytological data indicates that in spite of the low radiation dose, chimeras were established when a high number of parental type bone marrow cells were given; when BALB/c cells were given, the host's immune responses were not lowered enough by the radiation to allow the allogeneic bone marrow cells to survive and form chimeras.

64-839 LEUKAEMOGENESIS BY DMBA + X-IRRADIATION IN C57Bl MICE. (E., Abstract) Wallis, V. P. 116 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

All mice inj., s.c. within 24 hr. of birth with 60 μ g of 9,10-dimethyl-1,2-benzanthracene (DMBA) in 3% aqueous gelatin, and then given 4 weekly doses of 180 r X-rays for 4 wk., developed leukemia; while 90% of the mice that were irradiated only and none of those inj. with DMBA at birth only developed leukemia. The mean latent period from the last irradiation to the onset of leukemia was significantly reduced from 184 days in X-irradiated mice to 115 days in DMBA + X-irradiated mice. Those leukemias induced by X-rays only, grew as generalized leukemias, while the DMBA + X-ray-induced grew as solid s.c. tumors at the inj. site. When, in this strain of mice, DMBA is given in conjunction with a leukemogenic dose of X-rays, the leukemia incidence is higher than in mice irradiated only, and the latent period is decreased by about 40%.

64-840 A CLINICAL-PATHOLOGICAL CONFERENCE ON A CASE OF CARCINOMA OF THE BILE DUCT ASSOCIATED WITH DEPOSIT OF THOROTRAST. (Jap.) Yamagata, S. (Dept. Int. Med., Tohoku U. Sch. Med., Japan), T. Gomi, M. Satsuka, Y. Ito, Y. Katakura, H. Asakawa, K. Akasaki, N. Suwa, S. Arai and I. Watanabe. Saishin Igaku (Mod. Med.) (Osaka) 18(10):2357-2367, 1963.

Adenocarcinoma of the bile duct associated with deposit of Thorotrast in a 54-year-old Oriental male was discussed. Although no confirmatory history of injection of Thorotrast was obtained by the pt. and his family autopsy revealed the deposit of Thorotrast in the liver and spleen. Findings at autopsy included small and hard white-gray Thorotrast-containing nodules in the liver and the extensively atrophic spleen. The spleen was almost entirely displaced by a Thorotrast-containing whitish-gray substance.

See also abstract nos.: 819,826,828,864

CHEMICAL CARCINOGENESIS

64-841 INDUCTION IN RATS BY CELL-FREE FILTRATES PREPARED FROM BENZOPYRENE SARCOMAS.

(Ger.) Becker, P. (Max-Planck-Gesellschaft, Berlin-Dahlem, Germany) and E. Knake. *Zschr. Naturforsch.* 18b(12):1056-1059, 1963.

Cell-free filtrates prepared from s.c. sarcomas (induced in Wistar rats by inj. of benzpyrene) were inoc. i.p. into 0-5-day-old suckling rats of the same strain. Some animals received a single "challenge" dose of 9,10-dimethyl-1,2-benzanthracene (DMBA; 0.1 ml of a 0.025% soln. in sesame oil, s.c.) 7-8 wk. after inj. of the filtrate. After 11-24.5 mo., the following tumor rates were found: 2/147 treated with filtrate only had spindle cell sarcomas of uterus and thoracic wall, resp.; 3/55 inj. with filtrate and DMBA had tumors (2 sarcoma of flank, 1 liver cell carcinoma). Of the controls (animals of another strain), 4/789 untreated and 1/58 inj. with DMBA alone had tumors, but 2 of these were benign tumors. The presence of an oncogenic virus in the filtrates is therefore considered likely.

64-842 STUDIES ON THE DIFFERING EFFECTS OF CO-CARCINOGENS AND CARCINOGENS ON THE EPIDERMIS OF THE MOUSE. (Ger.) Dörmer, P. (Inst. Path., U. Freiburg i. Br., Berlin, Germany) and W. Oehlert. *Beitr. Path. Anat.* 129(2):307-330, 1964.

When the skin of Agnes Bluhm mice (18 g) was painted 1 or 5 times (at 24-hr. intervals) with various solvents such as benzene, cyclohexane or acetone or with croton oil in acetone, Substance A from croton oil, or Tween 60, use of thymidine- H^3 and colcemid revealed that there was an increase in the ratio of DNA-synthesizing cells and the number of dividing cells in the basal layer. This increase was even more pronounced when methylcholanthrene (MC; 0.25%) was added to the solvents. While in the hyperplastic tissue produced by the cocarcinogens the ratio of labeled cells over the mitotic count was the same as that determined in normal skin (about 10:1), MC-induced hyperplasia was characterized by a drastic shift in this ratio (30:1 after 1 application, 77:1 after 5 applications). These findings indicate that MC in combination with a cocarcinogen induces an uncoupling of DNA synthesis and mitotic activity, presumably due to inhibition of intermitotic cells in the G2-phase. When MC application was followed by repeated applications of Tween 60, this effect was no longer demonstrable. It is concluded that the transformation of normal cells into cancer cells is determined by 2 mechanisms: a cytotoxic factor and a proliferation-promoting factor. While both carcinogens and cocarcinogens promote proliferation, i.e., induce hyperplasia, only the former are also cytotoxic.

64-843 STUDIES IN THE MOUSE OF GENERATION TIME, DNA SYNTHESIS TIME, AND DURATION

OF MITOSIS IN CELLS OF HYPERPLASTIC EPIDERMIS AND SQUAMOUS CELL CARCINOMA AFTER TOPICAL APPLICATION OF METHYLCHOLANTHRENE. (Ger.) Dörmer, P. (Inst. Path., U. Freiburg i. Br., Berlin, Germany), H. Tulinus and W. Oehlert. *Zschr. Krebsforsch.* 66(1):11-28, 1964.

Weekly topical applications of 0.25% methylcholanthrene soln. in benzene to the dorsal skin of 19 adult Agnes Bluhm mice produced marked hyperplasia and some papillomas within 90 days, multiple carcinomas within 120-150 days. Autoradiographic studies using thymidine- H^3 were undertaken at each stage. In the hyperplastic and papillomatous tissue the life span of postmitotic cells was not prolonged as compared to that of normal, multilayered epithelium. Progressing carcinogenesis was marked, however, by a steady decrease in generation time, which was 150 hr. in normal epidermis, 56 hr. in hyperplastic tissue, and 32 hr. in squamous cell carcinoma. There was a corresponding increase in the rate of mitosis. The duration of DNA synthesis remained essentially unchanged (about 8 hr.), while the premitotic resting phase showed increasing fluctuation with progressing carcinogenesis, but did not exceed in length the phase of DNA synthesis. It is concluded that the most important change occurring in the transformation of a normal epidermal cell into a cancer cell is the shortening of the phase of differentiation of dividing cells.

64-844 PROLACTIN-RELEASING ACTIVITY OF 3-METHYLCHOLANTHRENE. (E.) Moon, R. C. (Dept. Physiol., U. Tennessee Med. Units, Memphis). *J. Nat. Cancer Inst.* 32(2):461-469, 1964.

A more complete report of the paper abstracted as CRA 1(6):#1099, 1963.

64-845 3-METHYLCHOLANTHRENE CONCENTRATION AND CLEARANCE IN SOME ADIPOSE TISSUES IN MICE. (E.) Hoshino, K. (Cancer Res. Lab., U. Western Ontario, London, Canada) and M. A. Bernet. *Cancer Res.* 24(4):648-652, 1964.

Female C57BL/6J mice (6-7 wk. old) were inj. once, i.p., with 1, 5, 10, and 20 mg of 20-methylcholanthrene (MC; in 1 ml of sesame oil) and killed 7 hr. later; other mice which received a single dose of 30 mg MC were killed 1-24 hr. after inj. Spectrophotofluorometric analysis of the mammary fat pads and interscapular brown fat pads of the mice showed that the following consistent relationship in MC conc. existed: fourth mammary fat pad < third mammary fat pad < interscapular brown fat pad. When examined 7 hr. after inj., the tissue conc. of MC had increased nonlinearly as the MC dosages increased linearly; in those that received 30 mg the peak conc. occurred 10 hr. later. Clearance of MC from mammary fat pads which had been isologously transplanted from donor mice 9 hr. after inj. of 30 mg of MC, was extremely

low; the tissue conc. 10 days after transplanta-
on was still slightly higher than that of the
controls. In another experiment using female
ALB/c x C3H/HE)F1 mice in which mammary paren-
chyma was removed from the mammary gland tissue,
the MC conc. was greater in intact fourth mammary
glands (including parenchyma) than in those which
were gland-free 7 hr. after a single inj. of
10 mg of MC.

846 DAMAGE TO THE THYMUS AND OTHER LYMPHOID
TISSUES FROM 3-METHYLCHOLANTHRENE, AND
SEQUENT THYMOMA PRODUCTION, IN MICE. (E.)
Suhira, K. (Stanford U., Palo Alto, Cal.).
Cancer Res. 24(4):558-569, 1964.

High toxicity was noted in newborn C57BL/Ka and
mice after a single i.p. inj. of 20-methyl-
cholanthrene (MC), 1.0 mg and 0.3 mg, resp.
Deaths within the first 10 days; deaths from
acute and chronic wasting disease and chronic
infection). Less toxicity was shown after inj. of
1 mg of MC into 1-6-day-old mice, but subsequent
inj. of 1 mg of MC/wk. resulted in lethal damage
in these animals. Mice over 7 days of age were
found to be resistant to MC damage. In C57BL
mice, growth of all animals was depressed; the
effect depended upon the dose and the age of the
mice. Histologic examination of these tissues
revealed conspicuous degeneration of young cells
in bone marrow, appearance of fibrolymphocytic
degeneration in spleen, lymph nodes and
thymus, with extensive pyknosis and karyorrhexis.
Leukemoid reaction was seen in 3 mice. In C3H
mice, among those which survived the initial
injection, 15 died between mo. 3-5 with greatly
enlarged thymuses (av. 590 mg; range 155-1270
mg). These thymomas were of 2 types: lympho-
cytic and stem cell. Among 4-month survivors
mice became emaciated and showed many lung
tumors; some developed malignant lung tumors
which resembled those of adenocarcinoma or
alveolar cell carcinoma. There were 2 cases
of leukemoid reaction.

847 FURTHER EXPERIMENTS ON THE CAUSE OF
SEQUENTIAL NEOPLASTIC CHANGES. THE
EFFECTS OF 20-METHYLCHOLANTHRENE ON TRANSPLANTED
DERMAL MOUSE PAPILLOMAS AND THE DERIVATIVE
CARCINOMAS. (E.) Henderson, J. S. (Rockefeller
Inst., New York) and P. Rous. *J. Exp. Med.*
122(2):197-221, 1964.

In crystalline 20-methylcholanthrene (MC) and
cells from tar-induced mouse epidermal papillomas
were inj. i.m. in mice (matched weanlings of C
strain), the papilloma cells were attracted by
the crystals and formed cysts around the crystals, allowing
them to escape only very gradually. The cancerous
cells present in the implanted material, however,
bonded far more actively to MC and took over
the papilloma growths. To prevent this, small
bits of papilloma tissue with MC crystals ad-
hering to them were implanted s.c.; the papillomas

were continually bathed in the gradually dissolv-
ing MC for many wk. Even with these favorable
conditions, MC neither increased the occurrence
nor the number of visible epidermal cancers de-
riving from the papillomas. It also failed to
cause sequential malignant changes in the car-
cinomas which developed.

64-848 NATURE OF THE RENAL LESIONS INDUCED BY
INTRAVENOUS INJECTION OF CARRAGEENAN.
(E.) Morard, J. C. (Res. Ctr. Immun. Allergy,
Paris, France), A. Fray, A. Abadie and L. Robert.
Nature (London) 202:401-402, 1964.

Rabbits receiving i.v. inj. of 50 mg of carrageenan
as a 1% soln. died after 48 hr.; their kidneys re-
vealed, macroscopically, signs of diffuse cortical
necrosis. Histologically, a fibrinoid-like sub-
stance was found to completely obstruct the glo-
merular capillaries. A few capillary thromboses
were noted in the spleen, liver, lung and myo-
cardium. Blood studies revealed a decrease in
total serum protein (plasma fibrinogen became un-
detectable) and a decrease in serum complement
level; blood urea-levels rose as did urinary pro-
tein; Hb appeared in the urine. Animals survived
treatment with 10 mg; discrete renal lesions
occurred. With 10 mg the most significant finding
was a decrease in the serum complement-level. In
guinea pigs inj. of 100 mg/kg of carrageenan pro-
duced immediate death; with 50 mg/kg death oc-
curred in 1 hr. Death occurred on the ninth day
after 5-10 mg/kg. Renal lesions similar to those
in rabbits were observed in guinea pigs and rats;
the lesions were less diffuse.

64-849 CELLULAR INJURY AND CARCINOGENESIS.
(E.) Magee, P. N. (Toxic. Res. Unit,
Med. Res. Council Lab., Carshalton, Surrey,
England) and K. Y. Lee. *Biochem. J.* 91(1):
35-42, 1964.

When 4 female rats (Wistar) were inj. with
n-butyl(¹⁴C)methylnitrosamine (75 mg/kg body wt.,
3 μ C), the incorporation of radioactivity (in
counts/min/cm²) found in RNA and proteins, resp.,
of the liver, kidney, spleen, and pancreas, was:
752 and 151; 186 and 110; 100 and 49; 3 and 264.
The ratio of specific radioactivity of RNA:protein
in these organs was higher with the n-butyl com-
pound (4:5) than with the tert.-butyl isomer
(0:53). Incorporation of radioactivity from
both isomers labeled in the butyl groups was
relatively very low. Specific radioactivity of
RNA and protein (counts/min/cm²), resp., in the
liver of female rats treated with C¹⁴-labeled
n-butyl(¹⁴C)methylnitrosamine and n-(1-¹⁴C)butyl-
methylnitrosamine (both 75 mg/kg, 6 μ C/rat) 7 hr.
after i.p. inj. was 1120 and 249; 11 and 46,
resp. Similar values 24 hr. after i.p. inj. of
75 mg/kg of tert.-butyl(¹⁴C)methylnitrosamine
(30 μ C/rat) or tert.-(2,2-¹⁴C₂)butylmethylnitros-
amine (15 μ C/rat) were, resp., 898 and 1681; 2
and 22. When specific radioactivity of RNA and

proteins of liver and kidney were measured at intervals of 8 hr. up to 48 hr. after i.p. inj. of (^{14}C)diethylnitrosamine (200 mg/kg, 8 μC /rat), max. incorporation occurred at 24 hr.

- 64-850 HISTOCHEMICAL DEMONSTRATION OF GLUCOSE-6-PHOSPHATASE IN TRANSPLANTABLE CHRYS-
OIDIN-INDUCED HEPATOMA. (E.) Małolepszy, J.
(Dept. Exptl. Oncol., Inst. Immun. Exptl. Therapy,
Polish Acad. Sci., Wrocław) and B. Peryt. Arch.
Immun. Ther. Exp. 11(1-2):115-119, 1964.

Glucose-6-phosphatase was histologically demon-
strated in the cytoplasm of the parenchymal cells
(trabecular and polymorphous) of transplantable
chrysoidin-induced tumors in C57BL and (C57BL x
R111) mice. Its enzymatic activity was the same
as that found in the liver.

- 64-851 EFFECT OF EDTA ON LEAKAGE OF PROTEINS
FROM SLICES OF NORMAL RAT LIVER AND
DAB-INDUCED HEPATOMA. (E.) Kalant, H. (Dept.
Pathol. Biochem., U. Toronto, Canada), R. K.
Murray and W. Mons. Cancer Res. 24(4):570-581,
1964.

The addition of 0.5% ethylenediamine tetraacetate
(EDTA) to a concentrated medium in which normal
rat liver was incub. significantly increased the
leakage of protein. While the addition of EDTA
to the concentrated medium specifically increased
the leakage of an unidentified material, "basic
protein 4", apparently derived from the microsomal
fraction, the medium without the addition of EDTA
revealed essentially the same electrophoretic
pattern of soluble proteins as that demonstrated
in whole liver. Slices of 4-dimethylaminoazo-
benzene (DAB)-induced hepatoma showed much more
variable leakage of protein, which was not con-
sistently or significantly increased by EDTA.
Almost all the soluble basic proteins, including
"basic protein 4", were markedly diminished or
absent from the hepatomas, and the presence of
EDTA in the medium did not alter their electro-
phoretic pattern. The findings confirm the
difference between the DAB-induced hepatoma cells
and normal liver cells with respect to the com-
plement of intracellular proteins and the in-
fluence of divalent cations.

- 64-852 MUTAGENIC ACTIVITY OF 4-HYDROXYAMINO-
QUINOLINE 1-OXIDE. (E.) Okabayashi, T.
(Shionogi Res. Lab., Shionogi & Co., Ltd., Osaka,
Japan), A. Yoshimoto and M. Ide. Chem. Pharm.
Bull. (Tokyo) 12(3):257-261, 1964.

Experiments using the W strain of Aspergillus
niger as a test organism have shown that 4-hydroxy-
aminoquinoline N-oxide (HAQO) possesses a muta-
genic activity similar to that of 4-nitroquinoline
N-oxide (NQO). This is significant in that the
biological reduction of NQO leads to the accumu-
lation of HAQO. (See also the following abstract.)

- 64-853 COLORIMETRIC DETERMINATION OF 4-HYDROXY-
AMINOQUINOLINE 1-OXIDE AND 4-AMINOQUINO-
LINE 1-OXIDE. (E.) Okabayashi, T. (Shionogi Res.
Lab., Shionogi & Co., Ltd., Osaka, Japan) and
A. Yoshimoto. Chem. Pharm. Bull. (Tokyo)
12(3): 262-267, 1964.

A method (modified Zucker-Nason) is described for
the determination of the microbial reduction pro-
ducts of 4-nitroquinoline N-oxide (NQO). The for-
mation of 4-hydroxyaminoquinoline N-oxide (HAQO)
and 4-aminoquinoline N-oxide, the major microbial
reduction products of NQO, were studied in this
manner. Large amounts of HAQO were found to
accumulate in the course of reduction. The reduc-
tion of NQO by washed cell suspensions of E. coli
and Aspergillus niger was also studied. (See also
preceding abstract.)

- 64-854 INCIDENCE OF MOUSE BLADDER TUMORS
FOLLOWING IMPLANTATIONS OF PARAFFIN
PELLETS CONTAINING CERTAIN TRYPTOPHAN METABOLITES.
(E.) Bryan, G. T. (Div. Clin. Oncol., U. Wisconsin
Sch. Med., Madison), R. R. Brown and J. M. Price.
Cancer Res. 24(4):582-585, 1964.

Pellets of paraffin wax implanted in the bladder
lumen of 38 mice induced only 1 carcinoma. A
similarly low incidence was found when 15-20%
suspensions of the following tryptophan metabolites
were incorporated into these pellets: 8-hydroxy-
quinoline, 8-hydroxyquinolinaldic acid, xanthurenic
acid and its 8-methyl ether, 4,8-quinolinediol,
L-kynurenine sulfate, 3-hydroxy-L-kynurenine and
3-hydroxyanthranilic acid. The apparently pro-
longed retention of these compounds in paraffin
(246-342 days) suggests that it is not a satis-
factory vehicle for testing the bladder carcino-
genicity of urinary tryptophan metabolites. (See
CRA 1(12):#2101, 1964 and the following two
abstracts.)

- 64-855 IN VIVO ELUTION OF TRYPTOPHAN METABO-
LITES AND OTHER AROMATIC NITROGEN COM-
POUNDS FROM CHOLESTEROL PELLETS IMPLANTED IN
MOUSE BLADDERS. (E.) Bryan, G. T. (Div. Clin.
Oncol., U. Wisconsin Sch. Med., Madison), R. R.
Brown, C. R. Morris and J. M. Price. Cancer
Res. 24(4):586-595, 1964.

See CRA 1(12):#2101, 1964. The rate of elution
was observed to follow first-order kinetics, and
a specific elution-rate constant (K) was calcu-
lated that provided a measure of the probable
extent and duration of exposure of mouse bladder
mucosa to potential carcinogens. (See also the
preceding and following abstract.)

- 64-856 MOUSE BLADDER CARCINOGENICITY OF CERTAIN
TRYPTOPHAN METABOLITES AND OTHER AROMATIC
NITROGEN COMPOUNDS SUSPENDED IN CHOLESTEROL. (E.)
Bryan, G. T. (Div. Clin. Oncol., U. Wisconsin Sch.
Med., Madison), R. R. Brown and J. M. Price.
Cancer Res. 24(4):596-602, 1964

Surgical implantation into the bladders of mice of suspensions of the following nitrogen-containing aromatic compounds in cholesterol pellets showed that these chemicals were not significantly more active than cholesterol pellets alone (carcinoma incidence 8%) in producing bladder carcinomas: 4,8-quinolinediol, kynurenic acid, 8-hydroxyquinoline-N-oxide, 2,8-quinolinediol, 2,6-quinolinediol, 2-naphthylacetamide, 2-nitronaphthalene and 2-amino-1-naphthol HCl. Significant carcinoma incidences were found, however, for the following: 8-methyl ether of xanthurenic acid, 33%; 3-hydroxy-L-kynurenine, 30%; 3-hydroxyanthranilic acid, 22%; 8-hydroxyquinolinaldic acid, 19%; N-acetyl-2-naphthylhydroxylamine, 23%; xanthurenic acid, 20%; 2-naphthylhydroxylamine, 29%; and N-hydroxy-2-acetylaminofluorene, 21%. (See also CRA 1(12):#2101, 1964 and the two preceding abstracts.)

64-857 PROTEIN-BOUND DYE AND PURINE-CATABOLIZING ENZYMES IN PARENCHYMAL AND NON-PARENCHYMAL CELLS OF RATS FED 4-DIMETHYLAMINO-AZOBENZENE. (E.) De Lamirande, G. (Montreal Cancer Res. Inst., Hosp. Notre Dame, Canada). Cancer Res. 24(4):742-750, 1964.

Analysis of two liver fractions, one rich in parenchymal cells and the other rich in non-parenchymal cells, of male Wistar rats (av. wt. 200 g) fed 4-dimethylaminobenzene (DAB; 0.06% conc.) showed that at an early feeding stage dye binding occurred at a faster rate in non-parenchymal than in parenchymal cells. Maximum binding in parenchymal cells was observed after 4 wk. Binding in nonparenchymal cells reached max. after 1 wk. of feeding and decreased afterward; a second peak was attained at the same time of the decrease in the amount of bound dye in parenchymal cells. Results on the activities of the purine-catabolizing enzymes show that a decrease in 5'-nucleotidase, inosine phosphorylase and uricase activities occurred in both parenchymal and nonparenchymal cells of the liver at early stages before liver cells became cancerous; the DAB diet did not greatly affect guanase activity. A more pronounced decrease in these enzyme activities was seen in the primary tumor. The possible relation between decreased enzyme activity and the induction of tumors is discussed.

64-858 RENAL TUMOURS IN RATS FOLLOWING INJECTION OF DIMETHYLNITROSAMINE AT BIRTH. (E.) Terracini, B. (Med. Res. Council Lab., Carshalton, Surrey, England) and P. N. Magee. Nature (London) 202:502-503, 1964.

Wistar Porton rats were inj. with 0.05 or 0.1 ml of a 0.25% soln. of dimethylnitrosamine (DMN; 125 or 250 µg). All that received the higher dose died before the end of wk. 2. Among 14/53 survivors past weaning (10 inj. when less than age 1 day, 4 when age 7 days) given 125 µg the

following neoplasms developed in 11 rats: 9 renal tumors (1 had both kidneys involved); 1 abdominal lymphoma; 1 hepatoma; 1 abdominal malignant lymphoma. The renal tumors (the first was observed in a rat that died at 36 wk. of age) were up to 8 cm in diameter and were all of the anaplastic type. No DMN could be recovered from rats 24 hr. after admin.; however, the rate of disappearance was slower during the first 12 hr.

64-859 RETENTION RATES OF PARTICULATE CARCINOGENS IN THE LUNGS. STUDIES IN AN EXPERIMENTAL MODEL FOR LUNG CANCER INDUCTION. (E.) Saffiotti, U. (Chicago Sch. Med., Ill.), S. A. Borg, M. I. Grote and D. B. Karp. Chicago Med. Sch. Quart. 24(2):10-17, 1964.

The retention rate (expressed as percent of inj. dose) in the lungs of Syrian golden hamsters following intratracheal admin. of dusts composed of 3,4-benzpyrene (BP; 5 mg) and hematite (45 mg) suspended in 0.5 ml saline, was found to decrease by a constant rate from the time of admin. to the end of the first wk. When 3.4 mg of BP was admin. to untreated animals or to animals pretreated with 3 mg/wk. x 9 of BP, the retention rates were the same for all animals but recovery values were higher for those in the pretreated group. After single doses of 23.0, 3.4 and 0.96 mg of BP, the percent recovery of BP was proportionally higher for the larger doses, but remained only slightly higher after the second day.

64-860 COMPARATIVE PATHOLOGY OF HUMAN BRONCHOPULMONARY CANCER AND THAT INDUCED IN MICE BY CIGARETTE SMOKE TAR. (Fr.) Kourilsky, R. and J.-L. Happert. Bull. Acad. Nat. Med. (Paris) 148(17-18):346-350, 1964.

When mice (Strains A, C3H and SWR; male; age 6 wk.) were inj. intrathoracically with extracts of tobacco tar (1% of that obtained from the combustion of the brown tobacco in one half of a cigarette and dissolved in 0.2 ml of physiological serum) every third day for 25 wk., signs of bronchopulmonary cancer appeared within 208 days in 50% of the cases and the incidence of malignant tumors increased eventually from 21.6% to 66.8%. The following properties of the bronchopulmonary cancer were similar in both mice and humans: sufficient doses and prolonged admin. before tumors appear; same appearance, infiltrative activity and incidence of bronchial stenosis; frequent hematologic alterations. The hematologic alterations appeared late in humans and early in mice and were not accompanied by anemia and suprainfection in the latter. A low incidence of metastasis (1/121 animals) was seen in mice as compared to humans.

64-861 LEUKAEMIA AND PHENYLBUTAZONE. (E.) Thorpe, G. J. (Sheffield 10, England). Brit. Med. J. 1(2):1707, 1964.

A case is reported of a woman (age 56 yr.) who, after having been treated with 100 mg phenylbutazone x3/day x 17 days for a painful, swollen left ankle, died three wk. later. Following a postmortem histological examination, the final diagnosis was acute leukemia. Taking into account the adverse effects of phenylbutazone reported by other investigators on other pts., the author concludes that the above case demonstrated a progression from hypoplasia of the marrow to acute leukemia.

- 64-862 HOMOTRANSPLANTATION OF EXPLANTED TISSUE. (E.) Swaen, G. J. V. (Lab. Viral Oncol., NCI, Bethesda, Md.). Transplantation 1(2):187-190, 1963.

Explants from aminofluorene-induced AxC rat hepatomas transplanted into R strain mice were either cultivated *in vitro* for 14 days in AxC medium (donor medium) or R medium (host medium) and then transplanted into R strain rats, or were transplanted directly into the host animals without previous cultivation. The percentage of "tumor takes" was 14.8% in the donor-cultivated, 18% in the host-cultivated and 2.6% in the non-cultivated hepatoma explants. No beneficial influence of the medium (isologous vs. homologous) upon the number of takes was apparent.

- 64-863 HAIR CYCLE AND CHEMICALLY INDUCED EPIDERMAL CARCINOGENESIS IN MICE RECEIVING LIOETHYRONINE. II. FINDINGS AFTER MULTIPLE APPLICATIONS OF METHYLCHOLANTHRENE. (E.) Weidenreich-Sherwin, R. (Dept. Dermatol., New York U. Sch. Med., New York) and F. Herrmann. Dermatologica (Basel) 128(6):483-490, 1964.

In the first of two experiments, Swiss albino mice (age 8 wk.; wt. 20-25 g) received 18 intrascapular skin applications (3x/wk. for 6 wk.) of a 0.6% soln. of 20-methylcholanthrene (MC) and s.c. inj. of a 0.25 ml soln. (24 µg/ml) of triiodothyronine (T3; liothyronine, 5x/wk. for 7 wk., starting one wk. prior to the first MC application). Control animals received the same MC applications, but no T3. Of 46 experimental and 51 control animals alive after 4 mo., there were, resp., 36/46 and 34/51 which bore tumors, 27/36 and 13/34 bore more than one tumor, 21/36 and 7/34 had more than two tumors and 26/36 (8 died with malignant tumors) and 24/34 (4 died with malignant tumors) had malignant tumors. In the second of the experiments, the mice were given MC 3x/wk. for 5 wk. and s.c. inj. of T3 5x/wk. for 12 wk. starting one wk. prior to the first MC application. Controls received the same MC applications and no T3. Of 48 experimental and 46 control animals alive after 4 mo., there were, resp., 37/48 and 21/56 which bore tumors, 25/37 and 7/21 bore more than one tumor, 15/37 and 2/21 had more than two tumors, and 11/37 (1 died with a malignant tumor) and 2/21 had malignant tumors. (See also CRA 1(8):#1460, 1963; and *ibid.*, 2(4):#689, 1964.)

- 64-864 CARCINOGENIC ACTION OF METALS. EFFECT OF METALS IMPLANTED INTRAMUSCULARLY INTO RATS. (E., Abstract) Heath, J. C. Pp. 389-390 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Injecting the pure powdered metals, nickel, cobalt, and cadmium (suspended in serum) into the thigh muscle of rats produced malignant, transplantable rhabdomyosarcomas at the inj. site. Histologically, the tumors produced by cobalt were least differentiated, those by nickel the best differentiated, while the cadmium tumors were intermediate. In other experiments to investigate the influence on the carcinogenicity of cobalt and the influence of the physical form of the metal, cobalt was introduced into the muscle in the form of polished spheres (2 mm in diameter; each approx. 37-38 mg); some were removed at 1, 2 and 3 mo. intervals. Biopsies showed no breakdown of the muscle into mononucleate myoblasts and no tumors either in the rats still bearing the cobalt or in those from which the explants had been excised. In contrast when powdered cobalt was implanted, of 28 mg originally inj., all had disappeared even at the microscopical level after 3-4 mo.; by this time the malignant change involving breakdown of the muscle fibers and proliferation of the mononucleate myoblasts had begun.

- 64-865 TESTS FOR MUTAGENIC ACTIVITY OF CARCINOGENS ON PHAGE T4 DNA. (E., Abstract) Alderson, T. Pp. 416-417 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

In an attempt to produce mutations in bacteriophage T4 DNA, *Escherichia coli* cells, singly-infected with T4 phage, were inhibited for protein synthesis and exposed to the carcinogenic hydrocarbon 1,2-benzpyrene. While under these conditions, phage DNA replicas were produced, but maturation and lysis did not take place; in consequence, naked phage DNA was exposed for several hr. to the hydrocarbon and then recovered by restoring protein synthesis to allow maturation and lysis. Although preliminary experiments by this method showed promise, these were not substantiated by later results.

- 64-866 ISONIAZID-INDUCED LUNG TUMOURS. (E., Abstract) Peacock, A. (Cancer Res. Dept., Royal Beatson Mem. Hosp., Glasgow, Scotland) and P. R. Peacock. Pp. 530-531 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Neither Wistar rats, hamsters nor desert rats (*Meriones libicus*), maintained on a standard pellet diet with 0.25% isoniazid in their drinking

water from June, 1962 until the time of this report, developed primary lung tumors. Since isoniazid-treated mice, however, quite frequently developed pulmonary papillary adenomas, the authors feel that this animal, therefore, possesses a peculiar factor not shared by the other species of rodents tested; this, presumably, makes the mouse particularly susceptible to isoniazid, urethan and possibly some other lung carcinogens.

64-867 BLOOD SUPPLY OF EXPERIMENTAL TUMOURS. (E., Abstract) Braithwaite, J. L. (Dept. Anat., U. Liverpool, England). Pp. 618-619 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

In the first of two series of experiments, all the vascular pedicles of a rat spleen were interrupted and when the spleen was completely devascularized a benzopyrene pellet was inserted into the middle segment. There was observed an atrophy of the infarcted spleen (though a capsule developed around the benzopyrene pellet) and regeneration of the splenic tissue from the dorsal mesogastrium which spread centrifugally. Also noted was the fact that a carcinogen implantation does not accelerate the appearance of a splenic tumor, nor its rate of growth from the time when it first becomes palpable. In the second experiment, two benzopyrene pellets were implanted into the spleen of the same animal, one into an infarcted zone and the second into a segment of spleen with an intact blood supply. In treated animals only one tumor developed, usually in the infarcted zone in the majority of the animals, although in a few the tumor was present in the segment with the intact blood supply. There was a lengthening of the latent period and retardation of the growth rate as compared with that found in the first series of experiments.

64-868 THE ORIGIN OF MAMMARY TUMOURS INDUCED IN RATS BY GASTRIC INSTILLATION OF DMBA. (E., Abstract) Foulds, L. P. 118 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Histological observations of mammary tumors in rats, formed by the intra-gastric instillation of 9,10-dimethyl-1,2-benzanthracene, showed these tumors to be carcinomas ab initio. They did not appear to originate in hyperplastic nodules or in plaques as do most spontaneous mammary tumors in inbred mice; however, an origin in nodules was not finally excluded.

64-869 MUTAGENIC INACTIVITY OF N-HYDROXY-URETHANE. (E., Abstract) Fahmy, O. G. and M. J. Fahmy. Pp. 131-132 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Genetic tests on the Drosophila testis with identical molar doses of urethan and its N-hydroxy-derivative, for the determination of the sex-linked recessive lethal rate, revealed that N-hydroxy-urethan is no more mutagenic than urethan. At a conc. of 0.43×10^{-2} M, the lethal rate for mature sperm (first 3 days progeny) was higher than that of control animals, but the mean rate for the whole of the germ line (18 days progeny) was not significantly different from the controls; at a conc. of 2×10^{-2} M, the mean lethal rate of the post-meiotic stages (sperms and spermatids) was not significantly higher than controls. A 5.6×10^{-2} M conc. was tolerated only with urethan and raised the mutation rate to 1.4% (approx. 7x above the control level).

64-870 EFFECT OF AUTOTRANSPLANTATION OF BENZO-PYRENE-INDUCED TUMOURS ON HOST RESISTANCE. (E., Abstract) Willoughby, H., A. Haddow, J. A. Stock, M. E. Whisson and M. Yarnell. P. 110 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Autotransplantation (s.c.) of sarcomas, which had been previously induced in rats by the s.c. implantation of pellets containing 3,4-benzpyrene, had in most cases a negligible effect on the growth rate of the primary tumor mass.

64-871 METABOLIC DERANGEMENTS IN HEPATOCARCINO-GENESIS. (E., Abstract) Reid, E. P. 81 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

In an attempt to note the salient changes in the levels and metabolism of nucleic acids and nucleotides during carcinogenesis, many derangements were observed, of which the following were deemed most important: (1) a greater NADPH₂ than NADP decrease, but neither being attributable to decreased synthesis as judged by assays for NAD-kinase; and no corresponding decrease in NAD; (2) an increase in glucose-6-phosphate dehydrogenase activity; (3) a channelling of carbamyl phosphate from urea synthesis into UMP synthesis; (4) an increased capacity of the "salvage" pathway for UMP synthesis, as judged by assays of uridine kinase; (5) increases in the levels of uridine nucleotides and decreases in the levels of purine nucleotides; (6) an increased capacity for dephosphorylation of UTP; (7) a decreased activity of the catabolic enzyme uracil reductase; (8) a decrease in RNA content particularly of the microsomal fraction and an increased proportion of guanine in the RNA of the supernatant fraction; (9) an increase in the acid-ribonuclease activity of the supernatant fraction; (10) an increase in RNA synthesis. The last two changes together are suggestive of a faster turnover of RNA.

64-872 BENZENE INTOXICATION WITH SYMPTOMS OF MALIGNANT RETICULOSIS. (Sp.)

Jiménez Díaz, C. (Inst. Clin. Med. Invest., Nuestra Señora de la Concepción Clin., Madrid, Spain), L. Lorente, G. Paniagua and M. Morales. *Rev. Clin. Esp.* 90(1):8-14, 1963.

The author presents 2 cases of men (age 55 and 37 yr.; both shoemakers by trade) with subleukemic infiltrating reticulosis who had been exposed to chronic benzene intoxication. Histologic examination revealed a proliferation of undifferentiated mesenchymal cells of varied aspect in the liver, spleen, bone marrow and some lymph glands of the pts. Also reviewed (19 references) are previously described manifestations (anemia, aleukemia, myeloid aplasia) of benzene intoxication (clinical and experimental).

64-873 ACUTE LEUKAEMIA ASSOCIATED WITH PHENYLBUTAZONE TREATMENT. (E.)

Woodliff, H. J. (Royal Perth Hosp., W. Australia) and L. Dougan. *Brit. Med. J.* 1:744-746, 1964.

In Western Australia investigation of 55 pts. with acute leukemia revealed that 8 had received phenylbutazone (P) treatment. In 5/8 cases the drug seems to be associated with the development of acute leukemia; in 2/8 X-ray therapy was also admin. and in 1/8 the drug was admin. only a short time before the leukemia became manifest. The incidence of acute leukemia in pts. treated with P is 9%; in a group of 417 pts. with chronic leukemia, lymphoma and allied disorders, 1.2% had received P in treatment. (See also the following abstract.)

64-874 PHENYLBUTAZONE THERAPY ASSOCIATED WITH LEUKAEMIA. (E.) Chalmers, T. M.

(Northern Gen. Hosp., Edinburgh, Scotland) and D. D. McCarthy. *Brit. Med. J.* 1:747, 1964.

A case history is presented of a 44-year-old woman who developed myelomonocytic leukemia after prolonged treatment with phenylbutazone (P; 100-300 mg/day in 3 courses varying in length from 6 mo. to 1 yr.). It is the first case reported in the literature of this type of leukemia occurring in association with P therapy. (See also the preceding abstract.)

64-875 IMMUNOLOGICAL CHANGES OF THE ORGANISM UNDER THE INFLUENCE OF CARCINOGENIC COMPOUNDS. (Rus.) Shapiro, D. D. (Ukrainian

Res. Inst. Industr. Hyg. Occupat. Dis., Kharkov, USSR) and I. Ia. Getmanets. *Biull. Eksp. Biol. Med.* 57(2):93-97, 1964.

Single s.c. admin. of 9,10-dimethyl-1,2-benzanthracene (DMBA; 40 mg) or multiple topical application (1 drop of a 1% soln. 2x/wk. for 4 mo.) to the skin of rabbits previously immunized with typhoid vaccine, resulted in a reduction of their

immunologic reactions. There was a tendency toward a decrease in gamma globulins. As expected, there was a decrease in agglutinin titer and an absence of blood acetylcholine; albumin increased and cholinesterase was markedly increased. When DMBA (as above) was admin. to either immunized or non-immunized rabbits in precancerous conditions, their skin reaction to serum of guinea pigs sensitized with serum of DMBA-treated rabbits also was increased.

64-876 MESENCHYMAL REACTIVITY IN ANIMALS BEARING THE WALKER TUMOR. AGAR- AND STARCH-INDUCED GRANULOMAS: OPTICAL AND ELECTRON MICROSCOPE STUDIES. (It.) Tedeschi, G. G.

(Inst. Gen. Physiol., U. Camerino, Italy) and M. Paparelli. *Oncologia (Basel)* 17(2):107-119, 1964.

Both optical and electron microscope studies were conducted on normal and Walker 256 tumor-bearing young adult Wistar WMZ male rats (wt. 200 g) after s.c. inoc. of agar (0.5 ml, 2% in distilled water) or starch (0.5 ml, 20% in distilled water). In normal rats, agar inoc. resulted in the formation of a nodular granuloma with extensive connective tissue tracts delimiting nests of macrophages forming syncytia and surrounding the strongly fragmented foreign body. In tumor-bearing rats, the inoc. of agar either s.c. or intratumorally (IT) did not cause granuloma formation but a few macrophage and collagenous connective tissue cells were seen. Starch inoc. into normal rats was followed by the formation of a plant-like granuloma composed of polygonal macrophages with foamy cytoplasm and with sparse collagenous stroma. In tumor-bearing animals, the inoc. of starch either s.c. or IT showed different macrophage structure (presence of plasmatic inclusion membranes) and pathologic collagen when compared to the reaction in normal rats.

64-877 THE AUTO- AND HETEROPLASTIC TRANS-PLANTATION OF EXPERIMENTAL TUMORS IN AMPHIBIANS. (It.) Leone, V. G. (Lab. Embryol. Exptl. Morphol., U. Milan, Italy) and T. Zavanella. *Tumori* 50(1):39-63, 1964.

Primary tumors were induced in adult newts (*Triturus cristatus*) by s.c. admin. of 2 mg of 20-methylcholanthrene crystals. Fragments of the tumor, or of its metastases, were then grafted into the eye or s.c. tissue of other adult newts of the same species, of another genus (*Pleurodeles waltlii*) and of anurans (*Xenopus laevis*). The tumor type observed in all cases was that of a junctional melanoblastoma, with different cell types noted in the anuran tumors. Tumor takes at graft sites showed no significant differences whether autografted (77%) or heterografted (82%); no significant differences were seen in the metastases reported for autografts (53%) or heterografts (67%). Metastases appeared early (after 12 days in some cases) and reached high

incidences in both eye and s.c. grafts: 50% after 1-2 mo. and 70-80% after 3-4 mo. Tumor takes and metastases (examined histologically), were as follows: 11/11 (100%) and 5/9 (55.6%) for newt → Pleurodeles; 19/21 (86.4%) and 16/22 (72.7%) for Pleurodeles → newt; 6/13 (46.1%) and 5/11 (45.4%) for newt → Xenopus; 9/9 (100%) and 9/10 (90%) for Xenopus → newt, resp. Metastases (percent) observed in Triturus, Pleurodeles and Xenopus were: for spleen, 53.2, 40 and 44.4; liver, 50, 30 and 44.4; heart, 26.1, 66.7 and 0; gonadal fatty bodies, 34.6, 33.3 and 0, resp. No significant differences were noted when the sex of the donor or host were considered.

64-878 IDENTIFICATION OF THALIDOMIDE IN RABBIT BLASTOCYSTS. (E.) Fabro, S. (Dept. Biochem., St. Mary's Hosp. Sch. Med., Paddington, London, W.2), H. Schumacher, R. L. Smith and R. T. Williams. Nature (London) 201:1125-1126, 1964.

Examination of blood samples and blastocysts taken from 10-day-old pregnant chinchilla rabbits 4 hr. after the admin. of ¹⁴C-thalidomide (6 mg/kg p.o.) revealed the following: significant amounts of radioactivity were found in all the blastocysts examined, although the conc. was generally less than that found in the maternal tissues; the ¹⁴C level in the blastocyst was approx. half that in the maternal blood; maternal tissue levels were similar to those of the blood, except for the liver where the conc. was 3-4x greater; more than 90% of the activity in the blastocyst was present in the yolk sac fluid and the other 10% in the embryo and yolk sac membrane; approx. 70% of the total activity was represented by T, 12% by α-(o-carboxybenzamido)-glutarimide and the rest by other primary and secondary hydrolysis products. While results do not indicate a direct casual effect between T and its toxicity to embryos, it is of interest to know that T and some of its products are present in the blastocyst at the time it is known to exert its teratogenic effect.

64-879 STUDIES ON THE TERATOGENIC EFFECT OF 2-DIETHYLAMINOPROPIOPHENONE. (Fr.) L. Lafon, R. (Lafon Res. Ctr., Maisons-Alfort, Seine, France), M. Sautai, J. Montagne and L. Personnier. Med. Exp. (Basel) 10(4):201-224, 1964.

After reviewing (46 references) various methods for studying the teratogenic effect of a drug, the authors emphasize the lack of a consistent screening technic. The chief effect of the admin. of thalidomide (50-250 mg/kg in 0.5-2.5% aqueous soln.) to 4-5-month-old mice and rats was reduction in litter size. The admin. of trypan blue (50-70 mg/kg p.o. of a 1% aqueous soln.) to Wistar rats resulted in a high degree of fetal resorptions and some fetal deaths. Vitamin A in doses of 20,000 I.U. p.o./Wistar

rat caused no increase in fetal resorption, while doses of 60,000 I.U. p.o./rat induced many fetal resorptions. Brain malformations were frequent in animals treated with trypan blue and vitamin A. The admin. of 2-diethylaminopropiophenone to rats (7-20 mg/kg) and mice (16.25-50 mg/kg) induced neither fetal malformation, resorption nor reduction of litter size.

64-880 CARCINOGEN-INDUCED MELANOTIC TUMOURS OF THE TYLOTRICH (HAIR) FOLLICLE. (E.) Straile, W. E. (Roswell Park Mem. Inst., Springville, N.Y.). Nature (London) 202:403-404, 1964.

Histologic examination of characteristic black spots arising in the skin of adult Syrian golden hamsters treated repeatedly with 9,10-dimethyl-1,2-benzanthracene showed that each spot was associated with a tylotrich follicle. The structure and innervation of these follicles are reported in detail. Numerous pigmented dendritic cells, corresponding to the perifollicular melanocytes described by Ghadially and Barker, were found scattered among the nerve endings and along the external sheath. Carcinogen-induced melanotic tumors arise at these particular sites.

64-881 CARCINOGENIC EFFECT IN GOLDEN HAMSTERS OF METHYLCHOLANTHRENE, BENZOPYRENE AND DIMETHYLBENZANTHRENE INJECTED AT DIFFERENT DOSES. (Fr.) Rivi re, M. R. (Lab. Exptl. Med., Inst. Cancer Res., Villejuif, Seine, France), I. Chouroulinkov and M. Gu rin. C. R. Soc. Biol. (Paris) 157(7):1364-1367, 1963.

Essentially similar to CRA 1(12):#2092, 1964.

64-882 POLLUTION OF THE NATURAL ENVIRONMENT BY POLYAROMATIC HYDROCARBONS OF THE 3,4-BENZOPYRENE TYPE. (Fr.) Mallet, L. Gaz. Hop. 136(16):803-808, 1964.

Surface soil samples taken from several wooded areas surrounding Paris, and from Orne and Seine-Maritime were measurably contaminated by 3,4-benzpyrene (BP; 0.4-12 µg/100 g), the deeper samples contained progressively more. In contrast, fallen oak leaves were strongly impregnated (30 µg/100 g). The areas closer to cities and industries were more highly affected, but even samples from Arctic pastures showed the presence of BP. Analyses were also made of various maritime inhabitants (µg/100 g dry wt.): eels, 0.15; clams, 0.25-2.5; oysters, 1.5-3.5; mussels, 0.3; scallops, 9. Discussion is also presented on various types of air pollution, with the conclusion that the elements of nature have not escaped contamination by BP. (See also CRA 1(6):#1062, 1963; and ibid., (8):#1493, 1963.)

64-883 ENZYMATIC N-HYDROXYLATION OF THE CARCINOGEN 2-ACETYLAMINOFLUORENE AND THE

METABOLISM OF N-HYDROXY-2-ACETYLAMINOFLUORENE-9-¹⁴C IN VITRO. (E.) Irving, C. C. (Dept. Biochem., U. Tennessee Med. Units, Memphis). *J. Biol. Chem.* 239(5):1589-1596, 1964.

Among the metabolites arising from the rapid metabolism of N-hydroxy-2-acetylaminofluorene (N-hydroxy-AAF; see CRA 1(5):#883, 1963), the carcinogens 2-acetylaminofluorene and 2-amino-fluorene have been identified. N-hydroxy-AAF is also metabolized by washed rabbit liver microsomes, but less rapidly, giving rise to 2 principal metabolites: 2-nitrosofluorene and azoxyfluorene. Studies on the enzymatic N-hydroxylation of 2-acetylaminofluorene are the same as reported in CRA 1(4):#691, 1963, except that the present report indicates that this process occurs also in the liver microsomes of the hamster, dog, cat, chicken, rat and mouse. The enzymatic formation of N-hydroxy-AAF by guinea pig or human liver microsomes was not detected.

64-884 BIOSYNTHESIS OF PYRIMIDINE DEOXYRIBONUCLEOTIDES IN HEPATOCARCINOGENESIS. (E., Abstract) Hartman, G. and E. Reid. Pp. 82-83 in *British Empire Cancer Campaign 1963*. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Assays of fetal liver, newborn liver, and primary hepatomas induced by 4-dimethylamino-3'-methylazobenzene (3'-Me-DMAB) showed activity of the order expected; no activity was detected in normal adult liver, or within the first few wk. of feeding of 3'-Me-DMAB, 4'-F-DMAB or ethionine. Slight activities have been encountered in two instances after rather prolonged 4'-F-DMAB feeding, there being distinct changes in the gross appearance of the liver. Similarly, the non-carcinogenic agent α -naphthylisothiocyanate gave no indication of an activity rise even though very extensive bileduct proliferation was a constant morphological finding. Results obtained from the thymidylate synthetase assay showed a very low rate of dTMP synthesis in normal liver (less than 1 μ mole/min./g fresh tissue). Primary hepatomas, and especially fetal liver showed high activity and a smaller rise was encountered in the first few wk. of feeding with 3'-Me-DMAB and 4'-F-DMAB. No rise was encountered with the non-carcinogenic agent α -naphthylisothiocyanate.

64-885 ELECTRON MICROSCOPE STUDY ON 2-AMINOFLUORENE CARCINOGENESIS. (Jap.) Kobayashi, E. (Dept. Otorhinolaryng., Sapporo Med. Coll., Japan). *Sapporo Igaku Zasshi* (Sapporo Med. J.) 23(3):178-193, 1963.

Groups of adult GIFU male rats (total, 63) were given 2-aminofluorene (AF), either 8 mg or 12 mg/day, p.o. When compared to azo dye carcinogenesis, less intense degeneration and necrosis of liver cells were observed. Electron microscopic study of the liver revealed that after

3 wk. the AF rats showed a fine vesicular agranular endoplasmic reticulum compactly aggregated in the cytoplasm. Changes in mitochondria were rather variable and less conspicuous than those in the endoplasmic reticulum. These findings relative to the endoplasmic reticulum are consistent with observations made after azo dye feeding, although the changes were less intense and less distinct. In the present experiment, no differences were noted in relation to the 2 doses of AF employed.

64-886 HISTOLOGICAL AND HISTOCHEMICAL STUDIES OF THE EARLY CHANGES OF RAT LIVER CELLS DURING 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE ADMINISTRATION. I. CHANGES OF RAT LIVER CELLS IN THE EARLY STAGES OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE FEEDING AND ITS INTRAPERITONEAL INJECTION. (Jap.) Jinnohara, T. (Dept. Path., Sapporo Coll. Med., Japan). *Sapporo Igaku Zasshi* (Sapporo Med. J.) 23(4-5):252-269, 1963.

After admin. of 3'-methyl-4-dimethylaminoazobenzene orally (12 mg/day) or i.p. (20 mg x 2) to adult GIFU rats, there occurred degeneration and necrosis of liver cells, especially in the central areas; these changes were, however, more intense after i.p. admin. In both cases these changes were apparent 24 hr. after initiation of dye admin. and reached its max. on the third day. Among histochemical changes noted were deformation, decrease or disappearance of RNA granules and changes in their distribution; hyaline bodies frequently appeared. During later periods there was absorption of necrotic areas, hypertrophy and regeneration of the liver cells and a transitional proliferation of bile ductules.

64-887 HISTOLOGICAL AND HISTOCHEMICAL STUDIES OF THE EARLY CHANGES OF RAT LIVER CELLS DURING 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE ADMINISTRATION. II. CHANGES OF RAT LIVER CELLS IN THE EARLY STAGE OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE ADMINISTRATION VIA STOMACH TUBING, INFLUENCE OF ITS INTERRUPTION, AND EFFECTS OF ADMINISTRATION OF PARA-HYDROXYPROPIOPHENONE ON THE TISSUE CHANGES. (Jap.) Jinnohara, T. (Dept. Path., Sapporo Coll. Med., Japan). *Sapporo Igaku Zasshi* (Sapporo Med. J.) 23(4-5):270-281, 1963.

When 2 groups of adult GIFU rats were fed intragastrically with 3'-methyl-4-dimethylaminoazobenzene (Me-DAB; 2 doses, each 4.8 mg or 4.8 mg/day x 14), there occurred at an early stage degeneration and necrosis of liver cells, especially in areas around the central veins. These changes were less marked when larger quantities were fed mixed with basic diet. In the second group, when the dye was stopped after 14 days, liver parenchyma was restored by proliferation of liver cells and by restoration of damaged cells. When p-hydroxypropiophenone (an antipituitary substance) was fed in the diet (0.4 g/day x 7) followed by 40 mg of Me-DAB (i.p., in 2 divided doses), there was an inhibition of the early changes induced by Me-DAB.

64-888 MALFORMATIONS INDUCED IN THE MOUSE BY THALIDOMIDE. (E.) DiPaolo, J. A. (Roswell Park Mem. Inst., Buffalo, N.Y.), H. Gatzek and J. Pickren. *Anat. Rec.* 149(1): 149-155, 1964.

Pregnant mice of inbred strains Swiss ICR/Ha, A/St and C3H/He, when given thalidomide (31-250 mg/kg by gastric intubation) for 4 or 5 days starting 6 or 7 days post-conception, showed congenital malformations in the offspring which included skeletal malformations of the long bones, head and trunk (seen in radiographs) and soft tissue malformations of the brain (seen in histologic preparations). The numbers involved were too small to detect strain differences in response.

64-889 RESPONSE OF THE GERMFREE (GF) RETICULO-ENDOTHELIAL SYSTEM (RES) TO CHEMICAL CARCINOGENESIS. (E., Abstract) Pollard, M. (Lobund Lab., U. Notre Dame, Ind.). *Fed. Proc.* 23(2)(Pt.1):393, 1964.

In various GF strains of mice (Swiss-Webster, ICR, CFW, C3H) with 20-methylcholanthrene (MC)-induced local s.c. fibrosarcomas, the regional lymph nodes were swollen. These and other nodes had germinal centers which were not detected prior to tumor. In contrast, in GF Sprague-Dawley rats with 9,10-dimethyl-1,2-benzanthracene-induced mammary carcinomas, while the lymph nodes were swollen, they contained no reaction zones. It is suggested that the difference in lymph node response in the 2 tumors is due to (1) the antigenic character of the tumor, (2) the sensitivity of the host reaction, or (3) the "unmasking" of an exotic agent by MC. (See also CRA 1(6):#1100, 1963; *ibid.*, 2(1):#30, 1964.)

64-890 INDUCED PROTECTION OF ADRENAL CORTEX AGAINST 7,12-DIMETHYLBENZ(a)ANTHRACENE. INFLUENCE OF ETHIONINE. INDUCTION OF MENADIONE REDUCTASE. INCORPORATION OF THYMIDINE-H³. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.) and R. Fukunishi. *J. Exp. Med.* 119(6): 923-942, 1964.

In reference to the adrenocorticolytic effects of 9,10-dimethyl-1,2-benzanthracene (DMBA; see CRA 2(2):#222, 1964), female Sprague-Dawley rats were given i.p. inj. of 25 mg of dl-ethionine (E) shortly before or after 2 mg i.v. of 20-methylcholanthrene (MC); DMBA was inj. i.v. 24 hr. later. The E blocked the protective effect of MC when it was admin. 1 hr. before or 1-2 hr. after the MC, whereas E alone was ineffective. In contrast, dl-methionine did not show this influence on aromatic protection. Enzymatic studies in the soluble fraction of liver homogenates showed that both DMBA and the aromatic antagonists induced an increase in the conc. of menadione reductase 3 hr. after admin. of 0.5-10 mg of MC, this enzymatic increase was proportional to the

dose and was also found in the adrenals, lungs, mammary glands and mammary cancer. The incorporation of tritium into washed residues of liver was reduced by i.v. inj. of DMBA; when given 4 hr. prior to thymidine-H³, the reduction was 56% of control values. This reduction was partially blocked by i.v. inj. of 2.5 mg of MC given 24 hr. previously. Protein synthesis and the extent of the damage to DNA seem to be 2 primary factors determining the protection provided by aromatic compounds. (See also CRA 1(9-10):#1714; *ibid.*, (12):#2065, 1964.)

64-891 AROMATIC INFLUENCES ON THE YIELDS OF MAMMARY CANCERS FOLLOWING ADMINISTRATION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.), L. Grand and R. Fukunishi. *Proc. Nat. Acad. Sci. USA* 51(5):737-742, 1964.

In order to relate dose and frequency of admin. to the number of mammary cancers evoked in normal female Sprague-Dawley rats, 9,10-dimethyl-1,2-benzanthracene (9,10-DMBA; i.v. lipid emulsion) was given: in 1 dose at day 50 (2-6 mg, 122 rats); 2 doses at days 50 and 53 (total dose 6 mg; 37 rats); or 3 doses at days 50, 53 and 56 (total dose 6 mg; 74 rats). All rats developed palpable cancers. When various protective hydrocarbons were fed to rats starting on day 47 prior to the i.v. admin. of three 2-mg inj. of 9,10-DMBA, the number of rats without cancer and the number of days before the appearance of tumors were as follows: 3/10 and 68 ± 23 for benzantracene (BA; 50 mg/day x 10); 3/10 and 70 ± 22 for 3',6-DMBA (5 mg/day x 10); 3/10 and 75 ± 18 for 4,5-DMBA (5 mg/day x 16); 4/10 and 73 ± 25 for chrysene (C; 15 mg/day x 16); 4/10 and 63 ± 19 for 1-methyl-7-isopropylphenanthrene (retene; 10 mg/day x 10); 6/10 and 44 ± 8 for 6-aminochrysene (5 mg/day x 15). Single doses of BA (20 mg) or C (40 mg) at day 48 afforded no protection. When 9,10-DMBA and 4,5-DMBA (0.1 ml of 2% (w/v) soln. in benzene) were inj. i.m. in a test of carcinogenicity without subsequent i.v. admin. of 9,10-DMBA, sarcoma was detected at the inj. site after 118 ± 15 and 115 ± 18 days, resp.; 3',6-DMBA did not evoke sarcoma.

64-892 ATTEMPTS TO INHIBIT CARCINOGENESIS BY 3,4-BENZOPYRENE (BP). (E., Abstract) Roe, F. J. C., B. C. V. Mitchley, T. A. Connors, M. Whisson, P. Alexander and D. I. Connell. P. 83 in *British Empire Cancer Campaign* 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Mice given 1% chlorazol yellow in their drinking water showed a slight delayed and reduced skin tumor response from induction by benzpyrene (50 µg x 2/wk. applied to the dorsal skin), whereas the response was increased when 1% titan yellow was given and was unaltered by 1% amaranth, 1% orange G, high doses of thiocetic acid (exact dosage not given) or whole body irradiation

(4 doses, total of 1100 r). However, in the latter case, a consistent difference in the macroscopic appearance of the malignant tumors was seen.

- 64-893 INDUCTION OF TUMOURS AT THE SITE OF THE SUBCUTANEOUS INJECTION OF THALIDOMIDE. (E., Abstract) Roe, F. J. C. and B. C. V. Mitchley. Pp. 83-84 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Repeated inj. of thalidomide (15 mg in 0.2 ml of arachis oil/wk. x 57) produced sarcomas at the site of inj. in 2/20 male Chester Beatty mice: only 5/20 remained alive at the end of this period. Controls inj. with arachis oil alone did not develop similar tumors. In another study, 1 of 3 mice developed a sarcoma at the inj. site during the 48th wk. after a total of 220 inj. were given, each 7.5 mg.

- 64-894 ONCOSTATIC PROPERTIES OF 1,3-OXAZINE DERIVATIVES. (E.) Chylinska, J. B. (Inst. Org. Synth., Polish Acad. Sci., Warsaw), E. Grochowski, M. Mordarski and T. Urbanski. Acta Un. Int. Cancr. 20(1-2):118-121, 1964.

In this study devoted to the chemotherapeutic effect of various dihydro-1,3-oxazine derivatives on s.c. Ehrlich tumors in R3 mice, it was noted that one compound (designated T 544) had a positive stimulating effect on the cancer.

- 64-895 SPONTANEOUS REPARATIVE PROCESSES IN BUTTER YELLOW-INDUCED CHRONIC LIVER DAMAGE. (Jap., Abstract) Akagi, Y. Kurume Igakkai Zasshi (J. Kurume Med. Assn.) 26(2): 183, 1963.

A diet containing 0.04% butter yellow (BY) was given for 3 mo. to albino rats, followed by a regular diet thereafter. The external surface of the liver had become granular with well-circumscribed gray nodules immediately after stopping admin. of BY. Histologically, these gray nodules showed a picture typical of adenoma; anisocytosis was also seen. The cytoplasm of bile duct epithelial cells was deeply stained, and there was hyperchromatosis of nuclei. One month after termination of BY, the hyperchromatosis and atypia were diminished but swelling and vacuolization of the cytoplasm and nuclei occurred. Two months after termination of BY, the irregularity of the liver surface and the gray nodules were significantly diminished or absent. The majority of bile duct epithelial cells had become hydropic, there was frequent vacuolization of nuclei, development of small round cells, and fibrotic changes near the degenerated epithelial cells of the bile ducts, indicating spontaneous reparative processes of BY-induced liver damage.

- 64-896 THE RELATIONSHIP BETWEEN DIMETHYLAMINO-AZOBENZENE (DAB) AS A CARCINOGENIC AGENT AND LIVER RNA IN THE RAT. (Jap., Abstract) Yo, S. (Dept. Biochem., U. Tokyo Sch. Sci., Japan) and H. Terayama. Seikagaku (J. Jap. Biochem. Soc.) 35(9):599, 1963.

RNA prepared from the liver of rats that had been pretreated with N-Cl⁴-methyl-DAB, had the same visible and UV absorption bands as normal RNA. It failed to absorb in the neighborhood of 400 mμ, eliminating the possibility that N-Cl⁴-methyl-DAB participated in the formation of azo dye compounds. Hydrolysis of each nucleotide revealed that the majority (80%) of radioactivity was located in guanine and adenine, indicating the possibility that the N-methyl derivative of DAB participated in the formation of purine.

- 64-897 ELECTRON MICROSCOPE STUDY OF CELL DEGENERATION AND PROLIFERATION. (X). MINUTE STRUCTURES OF AZO-DYE-INDUCED RAT HEPATOMA. (Jap., Abstract) Onoe, T. (Dept. Path., Sapporo Coll. Med., Japan), I. Suzuki, S. Hontani, H. Mori, M. Ezoe, T. Morita and H. Narimatsu. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Japon.) 52:164, 1963.

3'-MeDAB (12 mg/day mixed with food) was admin. to adult, male Wistar rats for 120 days. In 69/75 rats fed over 120 days, tumors developed in the liver. High protein diet and vitamin B admin. markedly inhibited the development of cholangiofibrosis. Microscopic studies showed that 15/69 developed typical hepatoma while the remainder had adenohepatoma. Cholangiocarcinoma was encountered in a few cases.

- 64-898 EXPERIMENTAL STUDY OF CARCINOGENESIS OF THE SALIVARY GLAND. (THIRD REPORT). (Jap., Abstract) Sugimoto, A. (Dept. Oral Path., Osaka U. Sch. Dent., Japan), T. Yagi, K. Okamoto, F. Taguchi, H. Hirawoka and K. Sakamoto. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Japon.) 52:242-243, 1963.

Carbowax pellets containing up to 20% 20-methyl-cholanthrene (MC) were implanted into the right maxillary gland of 30 adult Wistar rats (Group A). In another group of 30 rats similarly implanted with MC the excretory duct was ligated (Group B). Controls (45 rats) were subjected only to excretory duct ligation (Group C). The period of observation was 6-12 mo. In Group A, 13 developed carcinoma after 6-9 mo.; 2 of these showed lung metastases. Sarcomas developed in 3 rats (6-8 mo.); 8 showed benign tumors (6-10 mo.). In Group B, 4 developed carcinoma (6-8 mo.); 2 of these showed lung metastases. Three rats developed sarcoma (6-7 mo.) and 2 benign tumors (8-10 mo.). Adenomatous proliferation observed in Groups A and B appeared to change to carcinomatous proliferation accompanied by cyst formation, squamous metaplasia and keratinization due to the action of MC.

Histologically there appeared to be a continuum from benign proliferation to malignant proliferation. The ligation of the excretory duct did not appear to have any significant bearing on this carcinogenic process. Histologically malignant tumor types included epidermoid and squamous cell carcinomas, spindle cell adenocarcinoma and fibrosarcoma. Benign tumors included adenomatous epithelioma and papilloma.

64-899 HISTOPATHOLOGIC AND ELECTRON MICROSCOPE STUDIES OF EXPERIMENTAL MOUSE GLIOMAS AND THEIR TRANSPLANTS. (Jap.) Sato, K. (Dept. Path., Gunma U. Sch. Med., Japan). Kita Kanto Igaku (Kita Kanto Med. J.) 13(5):297-313, 1963.

After the intracerebral and intracerebellar implantation of pellets of 20-methylcholanthrene (1.5-2.5 mg) into 60 C57 Black mice and 75 C3H mice (1-3-month-old), 27(48%) and 22(30%) mice, resp., developed tumors (19 in the cerebellum) after 135-528 days. Tumor incidence was 32.7% in females, and 41.0% in males. Tumor types were 21 gliomas, 8 mixed glioma + sarcoma, 18 sarcomas and 2 unclassified tumors. Gliomas were characterized by cytological malignancy and mixed or transitional cell forms and thus, showed characteristics histologically different from those of human gliomas. Gliomas were further classified as: 10 glioblastomas, 3 oligodendroglioma-like tumors, 3 astrocytoma-like tumors and 2 ependymoma-like tumors. No medulloblastoma-like tumors developed. No significant correlation was observed between histological types and localization of gliomas. After implantation into mice, 28/32 tumors (including 14 gliomas) were successfully transplanted. By repeated transfers, the tumors came to show simpler types made up chiefly of atypical cells and some tumors even turned to sarcomas with extensive proliferation of mesenchymal components in the tumor stroma.

64-900 STUDY OF EXPERIMENTAL OSTEOSARCOMA INDUCED BY BERYLLIUM. (Jap., Abstract) Yamaguchi, S. (Dept. Path., Nagasaki U. Sch. Med., Japan) and H. Katsura. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Japon.) 52:229-230, 1963.

In rabbits, BeO (20 mg in saline) was inj. intramedullarily 2x/week for 1-43 wk. in the distal end of the femur. In 26/31 (84%) rabbits, chondrosarcoma, osteosarcoma, or a pre-sarcomatous state developed at the site of inj. or at the distant proximal end of the femur. In those which survived longer than 9 mo., the relationship between the number of inj. and the rate of tumor development was as follows: in those receiving 11-20 inj., tumor developed in 8/9 (89%); after 21-30 inj., tumor developed in 11/11; after 31-40 inj., tumor developed in 3/6 (50%); and in those receiving more than 41 inj., tumor developed in 4/4 (75%). The av. latent period for tumor development following the final inj. was 85 days. In 3 rabbits, sarcoma was confirmed histologically

but there was no gross evidence of a tumor. Metastases were seen in the liver, lymph nodes, and at other sites but were particularly frequent in lung (68%).

64-901 HYPOTHESIS ON THE ETIOLOGY OF CANCER. (PRELIMINARY NOTE). (Port.) De Mendonca, M. F. Folha Med. 48(3):41-44, 1964.

The author advances a theory according to which the ingestion of foodstuffs and drugs rich in Fe or S would tend to increase the production of H₂S (by the reaction $FeS + 2 HCl = FeCl_2 + H_2S$) which would in turn attack weak and traumatized points in the organism, thus conditioning these tissues for an easier development of neoplasias.

64-902 EPIDERMAL REACTION TO THE PRIMARY AND REPEATED ACTION OF 9,10-DIMETHYL-1,2-BENZANTHRACENE ON MOUSE SKIN. (Rus.) Pang, C.-L. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Vop. Onkol. 10(2):88-90, 1964.

After 2 applications of 3%, 9,10-dimethyl-1,2-benzanthracene (DMBA) to the skin of C57BL male mice, the extent of epithelial necrosis in mice given 10 preliminary applications of 0.05% DMBA was found to be less than that in controls topically treated with acetone only on days 2, 4, 6, 8 and 10. This difference was even greater in mice given 20 preliminary applications of DMBA while in those given 30 preliminary DMBA applications no necrosis was seen. It was thus shown that the sensitivity of the epithelium to DMBA varied according to the stage of carcinogenesis at the time of application.

64-903 EFFECT OF SOME PYRIMIDINE DERIVATIVES ON THE METASTASIZATION OF THE TRANS-PLANTABLE RAT SARCOMA SSK. (Rus.) Grekh, I. F. (Inst. Oncol., Acad. Med. Sci. USSR, Leningrad), R. S. Karlinskaia and I. L. Turbina. Vop. Onkol. 10(2):98-102, 1964.

Random-bred white female rats (60-100 g) were inoc. s.c. with 0.3 ml of 14-day old sarcoma SSK, tissue, and 24 hr. later treatment with various pyrimidine derivatives was initiated (100 mg/kg/day x 1-19, i.p.). 4-Methyluracil (MU), thymine, cytosine, and 4,6-dioxy-5-nitropyrimidine and isocytosine had no effect on the development of lung metastases. MU increased survival time, and did not promote an increase in the number and wt. of distant metastases. Thymine, cytosine or pentoxyl did not stimulate the formation of extrapulmonary metastases. Isocytosine, 2,6-dimercapto-5-amino-4-methylpyrimidine and dihydrothymine promoted the formation and growth of the metastases in lymph nodes. 4,6-Dioxy-5-nitropyrimidine had no effect on the formation of metastatic nodes.

64-904 SERUM LACTIC DEHYDROGENASE IN EXPERIMENTAL MOUSE LEUKEMIA. (Jap.) Asano, K.

(Dept. Int. Med., Okayama U. Sch. Med., Japan), T. Matsuura and M. Ono. Igaku To Seibutsugaku (Med. Biol.) 68(2):79-83, 1964.

When the dorsal skin of 18 one-month-old DbA mice were painted with 20-methylcholanthrene (MC; 5% benzene soln. 2x/wk. for 4 mo.), 14 (77.8%) developed lymphatic leukemia after latent periods of 50-100 days (av. 77 days). The serum lactic dehydrogenase (LDH) of these mice rose progressively almost in a direct relationship to the frequency of painting with MC. This rise of LDH which occurred around the sixth wk. after start of treatment was accompanied by pre-leukemic changes (leukopenia and hypoplastic changes in the spleen and the lymph nodes). The LDH went as high as 3,000-12,000 U (normally, 1,000-2,000 U). The LDH did not rise in those mice which had failed to develop lymphatic leukemia.

- 64-905 BINDING OF CARCINOGENIC AND RELATED AROMATIC HYDROCARBONS TO NUCLEIC ACIDS OF MOUSE SKIN, AND ITS PHYSICAL CHEMISTRY. (E., Abstract) Brookes, P. (Chester Beatty Res. Inst., Royal Cancer Hosp., London) and P. D. Lawley. Pp. 77-78 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Using an improved method of isolation and purification, previous results were confirmed showing that labeled, hydrocarbon carcinogens painted on mouse skin were found to be bound to particular cellular constituents. A correlation existed between the carcinogenic power (determined by Iball's index) and the extent of binding of the hydrocarbon to DNA: 1,2,5,6-dibenzanthracene (DBA), 3,4-benzpyrene (BP) and 20-methylcholanthrene (MC) were significantly bound to DNA, RNA and protein. With 9,10-dimethyl-1,2-benzanthracene (DMBA), the strongest carcinogen of those employed, the amount bound to DNA relative to that bound to RNA or protein was also the highest. Naphthalene was not bound to any cellular constituent, while 1,2,3,4-dibenzanthracene showed very low binding to DNA but appreciable binding to RNA and protein. The log of the equilibrium binding constant K obtained using salmon sperm DNA was: BP, 4.3; DBA, 3.4; and MC, 3.3. The binding was of a physicochemical nature since it was eliminated by the precipitation of DNA with alcohol.

- 64-906 EVIDENCE FOR THE BINDING OF POLYNUCLEAR AROMATIC HYDROCARBONS TO THE NUCLEIC ACIDS OF MOUSE SKIN: RELATION BETWEEN CARCINOGENIC POWER OF HYDROCARBONS AND THEIR BINDING TO DEOXYRIBONUCLEIC ACID. (E.) Brookes, P. (Chester Beatty Res. Inst., Royal Cancer Hosp.,

London S. W. 3) and P. D. Lawley. Nature (London) 202:781-784, 1964.

A detailed presentation of the work abstracted as CRA 2(5):#905, 1964.

- 64-907 THE INFLUENCE OF HEPARIN UPON THE METASTATIC SPREAD OF MALIGNANT TUMORS. EXPERIMENTAL STUDIES. (It.) Gallinotto, G. (Inst. Spec. Path. Surg., U. Pavia, Italy) and S. Zampogna. Minerva Chir. 19(10):347-349, 1964.

Adult rat of both sexes (wt. approx. 180 g), were treated with heparin sodium (H; 50 mg/animal i.v.) 15 min. before receiving i.v. inj. of 100,000 \pm 8,000 tumor cells from the Walker 256 carcinosarcoma. Of 70 animals treated with H, 20-29% showed lung metastases and 50-71% showed no lung metastases after 30 days; of 64 animals receiving tumor cells alone, 46-59% showed lung metastases and 18-31% showed none after 30 days. Thus, the implantation of tumor cells in the lung was seen to occur less frequently when H was admin. previous to the inj. of tumor cells.

- 64-908 EFFECTS OF THALIDOMIDE ON THE SKELETON OF THE RAT FOETUS. (E.) Klein Obbink, H. J. (Dept. Physiol. Chem., U. Amsterdam, The Netherlands) and L. M. Dalderup. Experientia 20(5):282-284, 1964.

When rats were fed thalidomide up to 2000 mg/kg daily from day 6 of pregnancy until the last day, the large bones of the extremities, shoulder, pelvis and ribs of the fetuses showed no anomalies. In general, the bones that show considerable variation in normal fetuses were most susceptible to the drug. Animals born of the 100-200 mg/kg groups showed marked anomalies in ossification of the cervical vertebrae, especially C₁, C₂, C₃ and C₄.

- 64-909 AN ELECTRON MICROSCOPIC STUDY OF A DIBENZANTHRACENE-INDUCED FIBROSARCOMA IN THE PIGEON. (E., Abstract) Pool, R. S. (Bowman Gray Sch. Med., Winston-Salem, N. C.). Fed. Proc. 23(2) (Pt. 1):337, 1964.

A fibrosarcoma induced in the pigeon by dibenzanthracene was composed of a single cell type. The elongated, spindle-shaped cell contained a moderate amount of endoplasmic reticulum of the rough variety and a moderate number of occasionally distorted mitochondria. The nuclei were larger than those of control cells and were more irregular and contained large irregular nucleoli and clumped electron-dense material. No tonofibrils or other specific organelles were noted. Collagen fibers were sometimes found along side of the tumor cells.

See also abstract nos.: 811,814,819,827,839,911

VIRAL CARCINOGENESIS

54-910 ISOLATION OF A REOVIRUS FROM A CASE OF BURKITT'S LYMPHOMA. (E.) Bell, T. M. (Imperial Cancer Res. Fund, E. African Virus Res. Inst., Entebbe, Uganda), A. Massie, M. G. R. Ross and M. C. Williams. Brit. Med. J. 1:1212-1213, 1964.

virus, antigenically related to reovirus Type 1, was isolated from a case of Burkitt's lymphoma and grown in a monkey kidney culture. This would appear to be the first recovery of reovirus in East Africa. Preliminary serological testing suggests a significantly higher incidence of antibody in lymphoma pts. than in healthy children. The implications of the serological testings are discussed.

4-911 EFFECT OF OROTIC ACID ON THE METASTASIS OF MAMMARY TUMORS IN MICE. (E.) Chu, W. (NCI, Bethesda) and R. M. Malmgren. Cancer Res. 24(4):671-673, 1964.

Female C3H/HeN mice were allowed to ingest mammary-tumor milk agent during the nursing period and then used for study at 5 mo. Treatment of the group with orotic acid (0.1% in drinking water) did not significantly alter the incidence of latent period of mammary tumors. However, 19% had foci of mammary tumor metastasis; 10% of controls had tumor metastasis in the lung. In a second study 117 mice (3 mo. old) received v. inj. in the tail vein of 0.25 ml of mammary tumor cell suspension. In 49 previously treated with orotic acid (1 ml 0.5% soln./day x 5, then 5 ml x 5 wk. throughout the experiment) microscopic lung metastases were observed in 42.8% compared to 17.6% in those which received only the tumor cell suspension.

4-912 SHOPE FIBROMA AND RABBIT MYXOMA VIRUSES. I. AUTORADIOGRAPHIC AND CYTOIMMUNOLOGICAL STUDIES ON "B" TYPE INCLUSIONS. (E.) Ito, S. (Dept. Pathol., Res. Inst. Microbiol., Osaka U., Japan), M. Takahashi, H. Miyamoto and J. Kamahora. Biken's J. (Osaka) 6(2):127-134, 1963.

Fluorescent antibody staining of human amnion (H) cells and embryonal kidney (ERK) cells infected with the Shope fibroma (Strain ATCB) virus (ter = 10⁶ Rabbit Infectious Doses) revealed the presence of fluorescent areas, which, when stained with Giemsa, appeared to coincide closely with "B"-type inclusions. Autoradiographic studies of FL cells or ERK cells inoculated with the Shope fibroma virus and rabbit myxoma virus and cultivated in a medium containing 10⁵ C/ml of H³-thymidine showed labeling of "B" type inclusions, but not of other cytoplasmic areas, and suppression of H³-thymidine incorporation into nuclei of inclusion bearing cells. It is concluded that the above inclusions are the site of viral antigen and synthesis of viral

DNA and are identical to inclusions already observed in other poxviruses. (See also CRA 2(3): #525, 1964.)

64-913 AN ELECTRON MICROSCOPE STUDY OF SARCOMA I IN A HOMOLOGOUS HOST. I. THE CELLS OF THE GROWING TUMOR. (E.) Chambers, V. C. (Dept. Microbiol., U. Washington Sch. Med., Seattle) and R. S. Weiser. Cancer Res. 24(4):693-708, 1964.

A comparison of the fine structure of Sarcoma I cells from the growing ascites tumors of C57BL/6K mice (homologous strain) with the fine structure of cells from the ascites tumors of A/Jax mice (isologous strain) showed no observable differences in the tumor cells grown in either strain of mice. There were occasional doughnut-shaped, virus-like bodies within cisternae of endoplasmic reticulum.

64-914 CORRELATION OF IMMUNOFLOURESCENCE AND INFECTIVITY IN THE DEVELOPING BOVINE CUTANEOUS PAPILOMA. (E.) Smithies, L. K. (Dept. Veterin. Sci., U. Wisconsin, Madison) and C. Olson. Cancer Res. 24(4):674-681, 1964.

Marked variation in susceptibility was noted among 14 calves (1-2 mo. old) who were inoculated intradermally (0.1 ml) and by scarification (approx. 0.05 ml) with papilloma virus preparations: 5/14 developed warts and 9/14 were resistant. Histologic development varied according to the route of admin.; warts induced by scarification regressed more quickly. Infectivity was correlated with the appearance of specific nuclear antigen (detected by the fluorescent antibody technic). Neither antigen nor virus, however, was found in the earliest stages of growth. The papilloma virus antigen location in nuclear material remained constant throughout development. Regression of the warts was accompanied by a decrease in specific antigen.

64-915 IN VITRO CULTURE OF YABA VIRUS-INDUCED TUMOUR FROM MONKEYS. (E.) Feltz, E. T. (U.S. Public Health Serv., Anchorage, Alaska). Nature (London) 202:625-626, 1964.

Minced tumor which developed after a second passage of Yaba virus (inj. s.c.) in a rhesus monkey grew in 4/14 cultures maintained at 37°C in medium 199 with 20% calf serum. This material produced typical Yaba virus tumors in monkeys; this tumor also could be cultivated *in vitro*. The cells appeared to be epithelioid or fibroblastic in structure.

64-916 LEUKAEMIA IN THE CAT. TRANSMISSION EXPERIMENTS WITH LEUKAEMIA (LYMPHOSARCOMA). (E.) Jarrett, W. F. H. (Veterin. Hosp.,

U. Glasgow, Scotland), W. B. Martin, G. W. Crighton, R. G. Dalton and M. F. Stewart. *Nature (London)* 202:566-567, 1964.

Of 4 kittens inj., s.c. (over the ribs) with 0.5 ml of a supernatant lymphosarcoma (obtained from a female cat (age 8.5 yr.) which had a lesion complex consisting of a large anterior mediastinal mass in the position of the thymus), 1/4 showed an advanced case of clinical lymphosarcoma at autopsy 15 mo. later. Histologically, the marrow showed heavy infiltration by neoplastic cells which contained virus-like particles. In tissue cultures made from the main mesenteric lymph node mass of the kitten and subcultured several times, the principal cell was similar to the neoplastic cells found in the histologic study. These findings may indicate the transmission of a spontaneous multicentric lymphosarcoma, though it is impossible to be completely sure that the inoculum did not contain a few living cells which survived freezing and homogenization.

64-917 LEUKAEMIA IN THE CAT. A VIRUS-LIKE PARTICLE ASSOCIATED WITH LEUKAEMIA (LYMPHOSARCOMA). (E.) Jarrett, W. F. H. (Veterin. Hosp., U. Glasgow, Scotland), E. M. Crawford, W. B. Martin and F. Davie. *Nature (London)* 202:567-568, 1964.

The virus particles found in the neoplastic cells of a cat (see the preceding abstract), upon electron microscope study, were found to consist of an electron-dense nucleoid enclosed in a densely stained double membrane; the outer diameter of the nucleoid measured about 60 mμ and that of the whole particle approx. 100 mμ. As yet no etiological relationship between the observed particles and the tumor has been established, but the similarity between these particles and the viruses of murine leukemia is striking.

64-918 EARLY CHROMOSOMAL CHANGES IN SV40-INFECTED HUMAN FIBROBLAST CULTURES. (E.) Wolman, S. R. (Dept. Path., New York U. Sch. Med., New York), K. Hirschhorn and G. J. Todaro. *Cytogenetics (Basel)* 3(1):45-61, 1964.

Prior to, or simultaneous with, cell transformation, the following karyotypic changes were seen the first few days after infection of slowly growing adult human skin fibroblasts (Strain A) with Simian virus (SV40) fluid: an increased number of chromosome and chromatid breaks, the appearance of dicentric chromosomes, an increase in tetraploidy, an accentuation of normally occurring secondary constrictions and the preferential loss of a member of the 6-X-chromosome group. Some of these alterations are due to the high frequency of telomeric associations seen.

64-919 INHERITANCE OF SUSCEPTIBILITY TO POLYOMA VIRUS IN MICE. (E., Abstract) Chang, S. S. (Dept. Med. Microbiol., U. California, Los Angeles) and W. H. Hildemann. *Genetics* 50(2): 240, 1964.

When the mode of inheritance of susceptibility to polyoma virus was investigated in neonatal F1 hybrids and reciprocal backcross progeny of the highly susceptible AKR/J and relatively resistant C57BL/6J lines of mice, it appeared that the susceptibility to tumorigenesis was determined by a single autosomal gene with incomplete dominance. At both low and high virus dosages, high but submaximal susceptibility of (AKR x BL/6)F1 hybrids was found, while only at high virus dosages was the recessive resistance of the C57BL/6 line overcome. The AKR line was highly susceptible to a runting syndrome which was associated with polyoma disease and was inherited recessively. The albino progeny of the F1 x AKR backcross were much more susceptible to runting than the black progeny. Susceptibility to runting was effected by interaction of the albino gene or one closely linked to it and another independently segregating gene also carried by the AKR line. The authors commented that other evidence suggests that early and efficient maturation of the immune response capacity is a major component of the genetic resistance to malignant infection associated with the C57 genotype.

64-920 MULTIPLE SELF-HEALING EPITHELIOMA. ELECTRON MICROSCOPY AND VIRAL STUDIES IN TWO CASES; NONSPECIFICITY OF A NUCLEAR PARTICLE IN KERATOACANTHOMA. (E.) Burket, J. M. (Dept. Derm., State U. Iowa Coll. Med., Iowa City) and R. M. Caplan. *Arch. Derm. (Chicago)* 90(1): 7-11, 1964.

Two cases of multiple self-healing epithelioma of Ferguson-Smith (MSHE) are reported. Electron microscopic studies revealed intranuclear particles which, at first, seemed to be identical to those described in solitary keratoacanthoma. These particles, however, have been shown to occur in entirely different cells and circumstances, rendering unjustifiable the possible identity of MSHE lesions with those of solitary keratoacanthoma, or the possible viral etiology of keratoacanthoma. The authors' attempts to culture a virus from lesions of the above two pts. failed.

64-921 BIOCHEMICAL STUDIES ON ADENOVIRUS MULTIPLICATION. VI. PROPERTIES OF HIGHLY PURIFIED TUMORIGENIC HUMAN ADENOVIRUSES AND THEIR DNA'S. (E.) Green, M. (Dept. Microbiol., St. Louis U. Sch. Med., Mo.) and M. Piña. *Proc. Nat. Acad. Sci. USA* 51(6):1251-1258, 1964.

When newborn hamsters were inoc. with adenovirus Type 12A (AT 12A; 0.25-6.0 μg), death within

25-60 days in 100% of the cases from tumors measuring 1-8 cm in diameter; tumors were induced with as little as 0.2 μ g. Tumor formation was prevented by rabbit antiserum (against purified Type 12A) but not by normal serum. When adult hamsters were inoc. with 5 μ g of AT 12A, either s.c., i.p. or intrapulmonary, no tumors had formed 15 mo. after inoc. Higher doses (2.5 μ g) and longer time periods were required to induce tumors with 3 other strains of Type 12 (12B, C and D) and with adenovirus Type 18A (AT 18A). No tumors occurred after inoc. with adenovirus Type 2 (3-30 μ g). Biochemical studies showed that AT 18A and 12A contain less DNA than the non-tumorigenic AT 2 and 4; the molecular wt. of DNA in AT 18A and 12A is 6-12% lower than that of the non-tumorigenic adenoviruses. (See CRA 1(4):#720; *ibid.*, #730; and *ibid.*, (8):#1568, 1963.)

64-922 SOME CHARACTERISTICS OF LARGE-PLAQUE AND SMALL-PLAQUE LINES OF POLYOMA VIRUS. (E.) Diamond, L. (Inst. Virol., U. Glasgow, Scotland) and L. V. Crawford. *Virology* 22(2):235-244, 1964.

Suspensions of small- and large-plaque lines of polyoma virus showed marked differences in the adsorption of virus particles to cells and to the hemagglutinin inhibitor released from the cells. Small-plaque virus was more readily adsorbed than large-plaque virus, and the difference could be used as an adjunct to plaque size distribution in determining the predominant plaque type of virus suspensions. The suspensions of a large- (33-4a) and small-plaque (43-4b) virus contained similar proportions of "full" particles of buoyant density 1.32 and "empty" particles of buoyant density 1.29. Another large-plaque strain (27-4c), however, showed a twice greater proportion of "empty" particles than the small-plaque strain. The large-plaque virus did not have hemagglutinating activity at 37° (pH 6.0-8.5), but did at 4° (pH 6.0-8.0), suggesting that at the lower temperature the virus might also adsorb to the inhibitor in a cell-free supernatant. Cells infected with small-plaque virus had a far greater fluorescent intensity than cells infected with large-plaque virus. Analyses of the viruses in individual plaques showed that the adsorption characteristics of both types of virus suspensions were stable properties that remained associated with their specific plaque type after plaque purification.

64-923 STRAIN DIFFERENCES IN NORMAL AND ABNORMAL PREGNANCIES IN MICE AND RELATIONSHIP TO MAMMARY TUMOR INCIDENCE. (E.) Hoshino, K. (Dept. Anat., Yale U. Sch. Med., New Haven, Conn.). *J. Nat. Cancer Inst.* 32(2):323-338, 1964.

Mice of the inbred strains CBA/SG (milk-agent-positive strain), C57BL/Jax (milk-agent-free-strain), BC₆G and their reciprocal hybrids,

were housed in a room maintained at $75 \pm 3^\circ\text{F}$ with a relative humidity of 30-40% throughout a 3-mo. observation period, at which time 1,882 pregnancies and 161 pseudopregnancies were observed. Of the 640 breeding mice, 330 had mammary tumors. Mammary tumor incidence in the CBA females was not altered significantly when they were outcrossed--between 34.3% and 23.5% ($P > 0.30$) and between 23.5% and 33.3% ($P > 0.30$)--though the av. age at which tumors appeared increased when they were mated with males of the tumor-resistant strains. The overall incidence of mammary tumors in CBA females in the breeding colony was 31.8%; the mice of the other two inbred strains, C57 and BC₆, which are mammary-tumor-resistant, had no mammary tumors when they were inbred or outcrossed. F₁ hybrid mice of groups CC₂ and BA₂, originating from CBA females, had mammary tumors of different incidence (78.8% and 22.6%, resp.; $P < 0.001$). The other two groups of F₁ hybrid mice, CC₁ and BA₁, derived from female mice of the C57 and BC₆ strains, resp., had no mammary tumors. Among all the mice, there was no relationship between mammary tumor incidence and any of the phenomena associated with pregnancy such as incidence of abnormal pregnancy, duration of normal and abnormal pregnancy and the duration of intravaginal bleeding.

64-924 STUDIES ON SPECIFIC TRANSPLANTATION RESISTANCE TO POLYOMA-VIRUS-INDUCED TUMORS. I. TRANSPLANTATION RESISTANCE INDUCED BY POLYOMA VIRUS INFECTION. (E.) Sjögren, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). *J. Nat. Cancer Inst.* 32(2):361-374, 1964.

Of 43 polyoma tumors tested for susceptibility to polyoma-virus-induced transplantation in various mouse strains, only 1, a thymoma morphologically similar to 4 other susceptible thymomas, showed no susceptibility. Only 2/35 nonpolyoma tumors showed resistance: 1 methylcholanthrene-induced sarcoma and 1 spontaneous mammary carcinoma. This resistance-inducing capacity was detected with dilutions 10^{-4} - 10^{-5} of the virus-containing substance and with partially purified virus preparations, but not with uninfected medium, indicating that the resistance effect is really induced by the polyoma virus and not by any other constituent of the virus-containing material. A good correlation was found between the induction of antiviral antibodies in the recipients and the transplantation resistance effect. (See also CRA 1(5):#898, 1963 and the 3 following abstracts.)

64-925 STUDIES ON SPECIFIC TRANSPLANTATION RESISTANCE TO POLYOMA-VIRUS-INDUCED TUMORS. II. MECHANISM OF RESISTANCE INDUCED BY POLYOMA VIRUS INFECTION. (E.) Sjögren, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). *J. Nat. Cancer Inst.* 32(2):375-393, 1964.

In addition to results previously reported in CRA 1(5):#898, 1963, neutralization experiments

involving the admixture of lymphoid cells or serum and complement to polyoma tumor cells were conducted. Lymphoid cells from donors infected with polyoma virus or pretreated with non-virus-releasing polyoma tumor cells were found to inhibit the growth of admixed polyoma tumor cells. Serum from polyoma-infected donors caused a more irregular and weaker inhibition. The inhibition in lymphoid cells is not a resistance effect, because it has been demonstrated in animals having no antiviral bodies in their sera. (See also the preceding and the following 2 abstracts.)

- 64-926 STUDIES ON SPECIFIC TRANSPLANTATION RESISTANCE TO POLYOMA-VIRUS-INDUCED TUMORS. III. TRANSPLANTATION RESISTANCE TO GENETICALLY COMPATIBLE POLYOMA TUMORS INDUCED BY POLYOMA TUMOR HOMOGRAFTS. (E.) Sjögren, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). *J. Nat. Cancer Inst.* 32(3):645-659, 1964.

Mice pretreated with any of 16 different polyoma tumor homografts showed resistance to polyoma tumor isografts given in the dose D_m (minimal cell dose for growth in 100% of untreated controls) or in a few experiments 10 or 100x this dose. Mice pretreated with 16 nonpolyoma tumor isografts showed no resistance. The methylcholanthrene-induced Sarcoma 64, shown previously to be susceptible to the polyoma-virus-induced resistance, was weakly susceptible also to the resistance induced by polyoma homografts and itself induced a weak resistance to polyoma tumor isografts (resistance to polyoma tumor 25 in 2/8 mice). Seven other nonpolyoma tumors tested grew equally well in all recipient categories. Only a resistance demonstrated in mice developing no antiviral antibodies was considered an indication of immunity induced by the tumor cells. Polyoma tumor cells X-irradiated with 8,000 r failed to induce the resistance. Eight polyoma tumor lines grew out in preirradiated recipients after inoc. of 2-50x lower cell doses than in irradiated animals, while 3 spontaneous mammary carcinomas grew equally well in the 2 groups. (See also CRA 1(5):#898, 1963; the 2 preceding abstracts and the following abstract.)

- 64-927 STUDIES ON SPECIFIC TRANSPLANTATION RESISTANCE TO POLYOMA-VIRUS-INDUCED TUMORS. IV. STABILITY OF THE POLYOMA CELL ANTIGEN. (E.) Sjögren, H. O. (Inst. Tumor Biol., Karolinska Inst. Sch. Med., Stockholm, Sweden). *J. Nat. Cancer Inst.* 32(3):661-666, 1964.

Thirteen single-cell clones of a polyoma tumor induced *in vivo* in adult mice showed like susceptibility to polyoma-induced transplantation resistance, indicating a homogeneous specific antigen content. The antigenicity of 2 tumors (SENSE sarcoma and polyoma TCSB) survived

unchanged serial passages, 42 and 19 times, resp., in virus-infected mice with a minimum superthreshold cell dose. In contrast, a methylcholanthrene-induced MCB sarcoma, also susceptible to polyoma-induced resistance, lost this property on 21 passages in virus-immune mice. (See also CRA 1(5):#898, 1963 and the 3 preceding abstracts.)

- 64-928 AN ATTEMPT TO DETECT AND TITRATE ROUS SARCOMA VIRUS PRODUCING CELLS OF RAT TUMOUR XC ON THE CHORIOALLANTOIC MEMBRANE OF THE CHICK EMBRYO. (E.) Vrba, M. (Inst. Exptl. Biol. Genet., Czech. Acad. Sci., Prague) and D. Chaytor. *Folia Biol. (Praha)* 10(1):50-53, 1964.

In an attempt to determine the proportion of Rous sarcoma virus (RSV) producing cells in the total cell population of the rat tumor XC grown *in vivo* and *in vitro* in tissue culture (TC) the chorioallantoic membrane (CAM) of White Leghorn chick embryos were inoc. with varying numbers of X-irradiated (5,000 r) XC tumor cells. When embryos (12 and 9 days old) were examined at 18 and 19 days of incub., different degrees of macroscopically determined proliferative centers were seen on individual CAMs: many in 12-day embryos inoc. with 3×10^5 irradiated cells grown *in vivo*; few in 9-day embryos inoc. with 6×10^4 irradiated TC cells; all negative in 9-day embryos inoc. with 1.5×10^5 irradiated cells grown *in vivo*. In another experiment, 10-day-old White Leghorn chicks of the same stock were inoc. with 3×10^5 , 3×10^5 , 1.5×10^5 , and 6×10^4 irradiated cells grown *in vivo* and 2/10, 1/4, 0/3, and 0/3, resp., died from tumors. When cell-free extracts of Rous sarcoma, XC from the rat and XC from CAM were inj. into chicks, the following tumors developed: 25/25, 0/44, and 2/37, resp.; latent period was 16 days for Rous sarcoma and 30 days for XC in CAM. The results of all the experiments indicate that the rat tumor XC contains only a small proportion of cells capable of virus production in contact with chicken tissue, although this capacity is genetically firmly established in the cell population of the tumor.

- 64-929 THE ROLE OF A SERUM FACTOR IN THE PRODUCTION OF HUMAN LEUKOCYTOSIS. (Hun.) Lehoczký, D. (Inst. Med. Sci., Budapest, Hungary) and F. Doctor. *Magy. Belorv. Arch.* 17(1):21-25, 1964.

The effect on leukocytosis was studied in groups of 3-4-month-old CBA mice after i.v. inj. with fresh serum from pts. with various diseases. Transient leukocytosis was seen in all mice which was due to handling and disappeared within 1 day. No sustained leukocytosis was seen in mice which received serum from normal pts. or were given saline. The serum of a pt. with cytopenia and hypersplenism produced a granulocytosis of 200% within 6-8 days. Serum of a pt. 12 hr. after heavy blood loss increased granulocytosis 115%; at the time this serum was taken, the pt's. own

hematopoietic system was not yet responding. Serum of a pt. with myelofibrosis and after splenectomy produced slight increases in neutrophil granulocytes at a time the pt. still had leukopenia. Serum of a pt. with toxic agranulocytosis treated with cortisone (200 mg/day) taken during the first and second day of treatment slightly decreased mouse WBC count, but when taken 6-8 days after start of treatment produced 65%-76% increases in leukocytes (only neutrophils). When this pt. started responding, his serum was no longer active. The bone marrow changes which preceded granulopoiesis in the pt. (promyelocytic hyperplasia) were reflected in the mice when active serum of the pt. was inj. Here again, marrow changes (increase of mitotic myeloid elements from 4/1000 to 20/1000) preceded peripheral granulocytosis. It is concluded that a factor in serum influences precursor cells in the bone marrow, and thus plays a role in the production of acute human leukocytosis.

4-930 ELECTRON MICROSCOPY. (E., Abstract) Milne, J. J. P. 567 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, W.I., 707 pp., 1963.

Electron microscopic studies of variously induced tumors in mice revealed no virus particles. A mouse tumor considered to be of thymic origin was found to contain large numbers of virus-like particles, somewhat hexagonal in section and of about 500 Å diameter. One mammary tumor from a Hf mouse contained large numbers of Type B virus particles; this was unexpected since this strain is presumably virus-free. Upon examination of other malignant tissues, Rous tumors were shown to be virus positive while tumors induced at supplementary cautery sites on affected rats appeared virus negative. There was one instance of a regressing Rous tumor being virus negative.

4-931 ANTIGENIC PROPERTIES OF LYMPHOMAS INDUCED BY THE MOLONEY AGENT. (E.) Klein, E. (Karolinska Inst. Sch. Med., Stockholm, Sweden) and G. Klein. J. Nat. Cancer Inst. (3):547-568, 1964.

In isologous hosts bearing the Moloney virus-induced lymphomas (ML), a specific transplantation resistance was established by pretreatment of the recipients with homografts of other ML, small homografts of the same lymphoma or virus-containing lymphoma homogenates. Extensive cross-resistance was demonstrated between different ML, but none was noted between ML and Gross-induced lymphoma (GL) or between ML and a number of virus-transplanted lymphomas. This resistance was paralleled by the appearance of humoral antibodies in the serum. Total body X-irradiation with 400 r reduced the minimum number of cells required for the take and growth of ML

cells after inoc. into untreated isologous recipients. Moloney target cells were killed only by anti-Moloney sera, but some hyperimmune anti-Moloney sera also killed cells of GL and long-transplanted lymphomas. It is concluded that ML differs (qualitatively?, quantitatively?) from other lymphomas in their antigenic specificity.

64-932 DETECTION OF SPECIFIC ANTIGEN IN SV40-TRANSFORMED CELLS BY IMMUNOFLUORESCENCE. (E.) Pope, J. H. (NIH, Bethesda, Md.) and W. P. Rowe. J. Exp. Med. 120(2):121-127, 1964.

When several SV40-transformed cell lines (hamster H50-1 and THK-1, C3H mouse kidney, rabbit kidney and porcine kidney) were combined with fluorescein-labeled antiserum (Anti-SV40), nuclear fluorescence was detected in each of the five cell lines upon immunofluorescent study. This serum also produced nuclear fluorescence in susceptible cells (AGMK or BSC-1) acutely infected with SV40 virus. In contrast, the antiviral serum gave no fluorescence with the SV40-transformed cells of hamster, rabbit or mouse origin but which contained no extractable virus. These findings provide evidence that cellular incorporation of the SV40 viral genome, subsequently expressed by at least one virus-specific antigen, is an integral property of all SV40-transformed cells.

64-933 IN VITRO MALIGNANT TRANSFORMATION BY POLYOMA VIRUS. (E., Abstract) Kirsten, W. J. Pediat. 65(1):109-110, 1964.

Benign and malignant neoplasms of epithelial and mesenchymal derivation, induced by the inj. of polyoma virus (PV) into newborn rats, hamsters, rabbits, and guinea pigs, varied according to the initiating dose and route of admin. A characteristic trait of lesions produced within 3 wk. after PV inoc. included cerebral, capillary and cavernous hemangiomas; bilateral renal sarcomas; and multiple exostoses of the ribs. Secondary monolayer cultures of embryonal rat kidneys were infected with large doses of PV and subcultured for 6-8 wk. From wk. 7 on, alterations, occurring in the growth pattern of the infected monolayers, were characterized by nodule formation, irregular cellular orientation, and cellular pleomorphism—changes suggestive of malignant conversion of the PV infected monolayers. When s.c. or i.p. transplantation of the transformed cell lines into adult inbred lines was attempted, the malignant lines proliferated continuously in the adult recipients forming large tumors at the site of inoc. Similar malignant transformation by PV, requiring 8-10 wk., was also accomplished in organ cultures of metanephric rudiments from 12-day-old rat embryos. Histologic features of the organ rudiments were similar to those of the renal sarcomas induced in vivo.

64-934 SHOPE FIBROMA AND RABBIT MYXOMA VIRUSES. II. PATHOGENESIS OF FIBROMAS

IN DOMESTIC RABBITS. (E.) Kato, S. (Dept. Path., Res. Inst. Microbiol. Dis., Osaka U., Japan), H. Miyamoto, M. Takahashi and J. Kamahora. Biken's J. (Osaka) 6(2):135-143, 1963.

The correlation between tumor formation, virus multiplication, inclusion formation and antibody response was studied in domestic rabbits (2 kg) inoc. with Shope fibroma virus (ATCB strain). When 10^6 rabbit infectious doses (RID)/ml of virus were inoc. intracutaneously, a palpable tumor appeared on day 4, reaching a max. size (30-50 mm in diameter) on about day 8 and disappearing completely in a mo. The virus titer of the tumor gradually increased for 10-12 days (occasionally up to 10^7 RID/g) and then rapidly decreased to zero on day 25. Inclusions, whose developmental form was similar to that of "B" type viral inclusions of other poxviruses, were exclusively found in the cytoplasm; they developed from a compact to a diffuse form, which seemed to cause degeneration of infected cells. The percentage of inclusion bearing cells in the total tumor cells in scratch preparations was about 40% at most; these became decreased to zero as early as day 10. A possible mechanism of tumor formation of fibromas is discussed.

64-935 LEUKAEMIA OUTBREAKS? (E.) Ollerenshaw, A. F. (Group Lab., Royal Infirm., Preston, England). Lancet 2:46, 1964.

A total of 33 acute leukemia pts. was seen in a laboratory serving a population of approx. 300,000 from January 1958-April 1964. Of these cases, only 7 occurred singularly at an interval of more than 3 mo. The others seemed to appear in clusters: 4 in January-March, 3 in September, 3 in June-July 1960; 4 in June-August 1961; 3 in September 1961-February 1962; 6 in August-October 1963; 4 in April 1964 presenting within a period of little over a wk. These recurrent outbreaks add affirmative evidence to the theory of a viral etiology for acute leukemia.

64-936 ISOLATION OF REOVIRUS IN BURKITT'S LYMPHOMA. (E.) Editorial Canad. Med. Assn. J. 90(23):1324, 1964.

Comment is made on various works: the isolation of virus from leukemia pts. by Negróni and his colleagues (see CRA 2(4):#720; and #721, 1964), isolation of a reovirus from biopsy material of a pt. with Burkitt's tumor (Bell, et al, see CRA 2(5):#910, 1964), recovery of 6 strains of virus from lymphomas in Kenya (see CRA 2(4):#723, 1964). The isolation of a virus, however, has not settled the important question of etiology (see CRA 2(4):#722, 1964). While it is too early to assume an etiological role for reoviruses in the Burkitt tumor, this possibility cannot be excluded.

64-937 HISTOCHEMICAL STUDIES OF LYMPHOMA CELLS INFECTED WITH POLYOMA VIRUS. (E., Abstract) Pearson, H. E. (U. South. California Sch. Med., Los Angeles). Fed. Proc. 23(2)(Pt. 1):401, 1964.

One to 3 days after infection of P388D1 murine lymphoma cells with polyoma virus the patterns of acid phosphatase (AP) and cytochrome oxidase (CO) was the same as in controls; after 5 days (during which time extensive cytolysis occurred) there was little or no AP, CO or lactic acid dehydrogenase (LAD). Cells which survived 3 wk. after infection were morphologically altered; some had relatively few and large AP granules, some had no CO or LAD granules. At 3 and 5 days (but not 1 day) after infection, cells incorporated less thymidine- H^3 than controls; cells after 3 wk. were like controls.

64-938 EFFECT OF SIMIAN VIRUS 40 (SV-40) ON PRIMARY CELL MONOLAYERS DERIVED FROM RHESUS MONKEY KIDNEYS. (E., Abstract) Easton, J. M. (NIH, Bethesda). Fed. Proc. 23(2)(Pt. 1):401, 1964.

A known SV40 virus strain (776) (as well as a naturally occurring contaminant strain) grew slowly but progressively in rhesus kidney monolayers, and destroyed them after several wk. When assayed on BS-C-1 continuous line cercopithecus cells, titers as high as 10^9 TCID₅₀/culture supernatant (6 ml) were obtained during the phase of rhesus cell degeneration. Cooling to 26°-28° inhibited viral growth and cell degeneration for several mo.; incub. at 36° resulted in high virus titers and destruction of the cell monolayers. The ultrastructure of these cells is similar to that of other cell types which undergo a more distinctive cytopathic effect from this virus. Viral particles, however, did not appear in the cytoplasm. (See CRA 2(1):#80, 1964.)

64-939 HOMOLOGY OF POLYOMA DNA TO DNA OF POLYOMA-FREE TUMORS. (E., Abstract) Axelrod, D. (NIH, Bethesda), E. T. Bolton and K. Habel. Fed. Proc. 23(2)(Pt. 1):401, 1964.

Tritium labeled polyoma viral DNA was sheared to produce uniform fragments of molecular wt. of about 600,000, heated and rapidly cooled, and incub. with polyoma-free tumor DNA, as well as with appropriate controls DNA embedded in an agar matrix. Homology was determined from the elution pattern of the radioactivity. Viral DNA binding to tumor DNA was greatly increased compared to normal DNA from the same source. Binding to bacterial DNA was not significantly greater than that for agar lacking DNA. The specificity of the binding of the viral DNA to the tumor DNA suggests the continued presence of at least one viral genome/cell in a state which may be analogous to that of the prophage in lysogenic bacteria.

64-940 SPECIFIC COMPLEMENT-FIXING VIRAL ANTIGENS IN HAMSTER AND GUINEA PIG TUMORS INDUCED BY THE SCHMIDT-RUPPIN STRAIN OF AVIAN SARCOMA. (E.) Huebner, R. J. (NCI, Bethesda), D. Armstrong, M. Okuyan, P. S. Sarma and H. C. Turner. Proc. Nat. Acad. Sci. USA 51(5):742-750, 1964.

Fibrosarcomas which were induced in newborn Syrian hamsters and weanling Hartley guinea pigs by s.c. inj. of S-R strain of avian sarcoma gave rise to complement-fixing (CF) antibodies in the serum of these animals. Serum antibodies increased in titer proportionally to the size of the tumor and/or time of exposure to tumor. These antibodies showed cross reactions with hamster "tumor" and chicken sarcoma "viral" S-R strain antigens. CF antigens were also demonstrated in preparations made from Bryan strain of Rous sarcoma and from standard strains of leukemia virus, such as RPL 12, erythroblastosis and RIF. The antigen reaction occurred only with serums of hamsters bearing S-R virus-induced tumors and not with serums carrying tumors induced by other oncogenic viruses, and appeared to be group-specific. Heating at 56°C reduced the antigen titers 16-fold or more. CF antigens were demonstrated in hamster tumor cells grown in tissue cultures which persisted through more than 20 serial passages of tumor cell transplants in hamsters, as well as undetermined generations of hamster tumor cells grown in tissue cultures. Neither of these tumor cell types yielded evidence of infectious virus. (See also CRA 1(9-10):#1740, 1964.)

64-941 THE RELATIONSHIP BETWEEN TUMOR VIRUS AND TUMOR CELL IN MOUSE BREAST CANCER AND LEUKEMIA. (Jap.) Awano, G. (Dept. Int. Med., Fukushima Pref. Coll. Med., Japan), S. Sotojima, S. Matsuyama, I. Takahashi and H. Sato. Nippon Naika Gakkai Zasshi (J. Jap. Soc. Intern. Med.) 52(5):521-522, 1963.

When tissues of C58 and AKR mice with spontaneous leukemia and the spontaneous breast tumors of C3H, C58 and dd mice were examined, virus inclusion bodies were found in all cases. After long-term, repeated transplantation of the mouse leukemia, while transplantation characteristics did not change, the virus bodies were more difficult to find. When these mice were X-irradiated (200 r) and then occasionally transplanted, the virus inclusions again became evident. (See also CRA 1(9-10):#1734, 1964.)

64-942 DISTRIBUTION OF INFECTIOUS VIRUS AND VIRAL ANTIGEN IN RATS AND MICE INFECTED WITH ROUS VIRUS. (Rus.) Kriukova, I. N. (N. F. Gamaleya Inst. Epidemiol. Microbiol., Acad. Med. Sci. USSR, Moscow) and I. B. Obukh. Vop. Onkol. 10(3):3-8, 1964.

Embryo or newborn rats (Wistar) or newborn mice

(including strain C57BL and C57BL/10Sn) were infected with Rous sarcoma (strain Carra; titer 1:104, 1-2 inj., 0.2 ml for rats, 0.1 ml for mice, i.p.). In rats with hemorrhagic disease infectious form of Rous virus (RV) was seldom found. Viral antigen was mostly observed in immature cyst walls, liver and lymph nodes; RV was not found in 3 sarcomas. While RV multiplies in rats, only rarely does it attain full maturation. The comparison of fluorescent antibody data, data on irradiation of tissue of infected animals and examination of the sera on the content of virus neutralizing antibodies, permit the conclusion that a more complete form of integration of RV with the cells takes place in the rats than in rabbits. RV was rarely found in mice.

64-943 THE CHLAMYDATE FORM OF LEUKEMIA VIRUS. (Sp.) Mas y Magro, F., Jr. (Inst. Exptl. Cytol. Hemat., Alicante, Spain). Sem. Med. (B. Air.) 123(21):813-817, 829, 1963.

A suspension of material taken from the blood, bone marrow and lymph glands of pts. with chronic lymphoid leukemia was inoc. *in vivo* into scarified areas of the right dorsal region of guinea pigs, and smears of the material appearing in the inoc. area taken 14, 28 and 42 hr. later revealed numerous proliferating chlamydate viral forms. Under oil immersion (magnification = 2,000-2,500 diameters; Giemsa stain) these appear stained in bright metachromatic red surrounded by a bluish gray envelope, which is the "chlamydia", or mantle, proper. The chlamydate forms appear upon fluorescent microscope examination (aurothioglucose staining method) as a light green fluorescence on a dark background and, at times, show an annular structure; they are always intracellular, and are localized exclusively in myeloblasts and lymphoblasts. Their total dimensions are between 3.2-5 μ and their central corpuscle measures 0.9-3.8 μ . The annular forms, with light staining centers, represent advanced stages of evolution. The chlamydate form of the leukemia virus seems to be a symbiotic form which allows adaptation to parasitic life and usually appears in cells which have undergone vacuolar degeneration and lysis of the nucleoplasm.

64-944 CYTOPATHIC CHANGES IN HUMAN FORESKIN CELLS INDUCED BY SIMIAN VIRUS. (E., Abstract) Petursson, G. (Sloan-Kettering Inst. Cancer Res., New York) and J. Fogh. Fed. Proc. 23(2) (Pt. 1):401, 1964.

Cytopathic changes in living unstained cultures of human fibroblastic cells 8-11 days after infection with SV40 (strain VA 45-54 GMK 5) included large, elongated, multinucleated cells. Fixed and stained preparations showed changes in the nucleus of a few cells starting at day 3; there was an increase in nucleolar size, swelling of nuclei with coarsening, clumping and margination of chromatin leading to pyknosis and cell death. Inclusion

bodies with halos were seen in some cells, as was cytoplasmic vacuolization. Most common cytoplasmic changes were retraction, granularity and increased affinity for eosin. After 3-4 wk. destruction was extensive with few surviving cells; some were multinucleated. These cells have shown no evidence of dividing or of increased metabolism several mo. after infection.

64-945 AN ANALYSIS OF A QUANTITATIVE STUDY ON NATURALLY OCCURRING ANTIBODY WHICH NEUTRALIZES ROUS SARCOMA VIRUS IN DIFFERENT GENETIC LINES OF CHICKENS. (E., Abstract) Bower, R. K. (Wadley Res. Inst., Baylor U., Dallas, Tex.), N. R. Gyles and C. J. Brown. Texas Rep. Biol. Med. 22(1):222-223, 1964.

The chorioallantoic membranes (CAMS) from 711 White Leghorn chick embryos were examined for tumors induced by Rous sarcoma virus (RSV) 7 days following inoc. of virus mixed with 3 dilutions of the serums from 58 dams, representing 3 genetic strains of chickens. Analysis of the combined data showed highly significant differences between breeding groups, dilutions of serum and interaction of breeding group and dilution of serum ($P = 0.01$). Analysis by least squares estimates showed that the smaller av. number of virus-induced tumors on CAMS which received serum from White Leghorn dams was highly significant compared with either Jungle Fowl-Cross or Giant Jungle Fowl dams. These differences were consistent with the finding of higher levels of neutralizing antibodies for RSV in White Leghorn dams. (See CRA 2(2):#285, 1964.)

64-946 ASCITES TUMOURS FROM BHK.21 CELLS TRANSFORMED IN VITRO BY POLYOMA VIRUS. (E.) Sanders, F. K. (Med. Res. Council Lab., Carshalton, Surrey, England) and B. O. Burford. Nature (London) 201:786-789, 1964.

After inoc. in young adult hamsters of 5×10^6

BHK cells of a polyoma-transformed clone (C.13/TC.6) the s.c. tumors obtained when successively transplanted i.p. into hamsters ultimately gave rise to some small solid and ascites tumors in the mesentery and peritoneum of 2 hamsters. At autopsy each yielded approx. 10 ml of bloody ascites, containing $3-5 \times 10^8$ tumor cells. No tumors were obtained from the untransformed BHK/C.13 cell line. No ascites tumors were found upon i.p. inoc. of 1×10^7 cells of transformed BHK/C.13/TC.6 cell line. Characteristic high plating efficiencies resulted from the ascites cell line when grown in agar medium. Subsequent susceptibility tests demonstrated that BHK ascites cells appear insusceptible to enteroviruses (including all 3 types of poliovirus), to both A and B coxsackie viruses, to polyoma virus, to Rous sarcoma virus and to adenovirus Type 12 and of doubtful susceptibility to yellow fever, West Nile and a number of arbor-viruses. Susceptibility in vitro was shown to the following viruses: EMC, Semliki forest, equine encephalomyelitis, echo 10, reoviruses II and III, Sendai, fowl plague, adenovirus Type 5, rabies, herpes and vaccinia.

64-947 POLYOMA VIRUS STRAINS OF DIFFERING ONCOGENICITY: TRANSPLANTATION IMMUNITY IN MICE. (E.) Friedman, R. M. (Natl. Inst. Med. Res., Mill Hill, London, N. W. 7) and A. S. Rabson. Virology 23(2):273-274, 1964.

Nine days after i.p. infection with $10^{3.7}$ TCID₅₀ of M or S variant of polyoma virus, C57BL/6JN mice were inoc. s.c. with various dilutions of viable C57-695 fibrosarcoma cell suspensions derived from the 32nd passage of an SE polyoma virus-induced tumor. The resistance to this challenge produced by the M or S variant required 10 times as many tumor cells to produce a successful tumor transplantation. However, the degree of this resistance was the same for these 2 variants despite their remarkably different oncogenic potential. (See also CRA 1(12):#2136, 1964.)

See also abstract nos.: 811,814,819,827,839,911

EPIDEMIOLOGY AND BIOMETRY

- 64-948 CLINICAL AND DIAGNOSTIC ASPECTS OF MALIGNANT MELANOMAS. (Ger.) Sinner, W. (Clin. Radiotherap., U. Zurich, Switzerland). *Oncologia (Basel)* 17(2):135-158, 1964.

A review of the literature (57 references) is supplemented by an analysis of 145 cases studied or treated by the author. Among the author's cases, no evidence of hereditary factors was found, but malignant degeneration of pigmented nevi existing from childhood was demonstrated in 38.6%. The danger of exacerbation through trauma is stressed, and all traumatizing diagnostic or therapeutic interventions are considered contraindicated. Spontaneous microtraumas were demonstrated in 29.5%, "provoked" macrotraumas in 15.9%, and diagnostically produced traumas in 16.6%. The etiological role of hormonal factors is also discussed briefly. The relatively low incidence of malignant melanomas is documented by the fact that the 145 melanomas constituted 1.16% of all malignant tumors among 12,262 cases treated. The age incidence curve reached a first peak in the fourth decade, a second peak at the beginning of the seventh decade. The male:female ratio was 1.5:1. Most frequent sites of the tumors were trunk (27.5%), head and neck (22.6%), lower extremities (22%), upper extremities (14.4%), and eyes (8.9%). Metastases were most frequently located in lymph nodes, skin, and lungs.

- 64-949 PREVENTION OF CANCER IN PATIENTS WITH GASTRIC POLYPS AND POLYPOSIS. (Cz.) Skler, J. (2nd Clin. Surg., Fac. Med., Charles Univ., Prague) and M. Pospíšil. *Cesk. Gastroent. yz.* 18(4):257-260, 1964.

Among 26 pts. operated upon for gastric polyps, 12 suffered from carcinomas which developed from the original benign adenomatous polyps. In two pts. where simple excision of benign polyps was performed, death from gastric cancer followed within 4 and 5 yr. after operation.

- 64-950 HERPES ZOSTER AND CANCER. (E.) Moynihan, N. H. *Practitioner* 192:69-673, 1964.

The author presents case histories of 4 pts. (2 male, 2 female, age 54-57 yr.) who developed malignant disease (3/4 bronchial carcinoma and 1/4 epidermoid carcinoma) and who were heavy smokers; 1/4 epidermoid carcinoma of the right tonsil) out of 23 cases (8 male, 15 female; age 13-82 yr.) of herpes zoster seen in his practice from 1960-62. He concludes with a review (26 references) of similar herpes zoster-malignancy transformations encountered in the literature.

- 64-951 RECENT TRENDS IN CHILDHOOD CANCER. (E.) Editorial. *Statist. Bull. Metrop. Life Insur. Co.* 45:2-5, 1964.

Significant changes in the death rate (per million) of children with malignant neoplasms have not been noted in white children under 15 yr. of age for the periods 1949-51 (95.6 males; 77.0 females) and 1959-61 (94.3 males; 73.9 females). In large measure, mortality trends of children with malignant neoplasms parallel most closely the mortality trends observed in leukemia, which accounts for approx. 50% of the total cancer mortality under age 15. The leukemia death rate among white boys decreased from 43.3 to 29.2 under age 1 and from 68.7 to 63.4 at ages 1-4; in contrast, the rates at ages 5-9 and 10-14 increased from 38.8 to 49.0 and from 26.4 to 31.0, resp. Parallel trends were seen among white girls. According to type or site of cancer, frequencies in white boys as compared to white girls under age 15 for 1959-61 were, resp., leukemia and aleukemia, 46.2 and 35.0; lymphosarcoma, 8.3 and 3.8; Hodgkin's disease, 1.7 and 0.7; cancer of the g.i. tract, 2.0 and 1.8; cancer of the genital organs, 0.9 and 1.3; eye cancer, 1.0 and 0.8; cancer of nervous system, 19.4 and 16.2; bone cancer, 3.1 and 3.7; urinary tract cancer, 5.1 and 5.5.

- 64-952 CANCER IN CALIFORNIA, 1942-56. (E.) Linden, G. (California Tumor Registry, Berkeley), K. Bragg, J. E. Dunn, Jr. and L. Breslow. *Public Health Rep.* 79(4):346-350, 1964.

A study of cancer in California based on a total of 110,229 cancer cases initially diagnosed in 37 hospitals between January 1, 1942 and December 31, 1956, and reported to the California Tumor Registry. The percentage of cancer which was localized varied from site to site (13%, pancreas to 94%, skin). Whites had a higher proportion of localized cases than other groups; Chinese and Japanese had a higher proportion in inaccessible sites. The frequency of stomach cancer to all cancer decreased between 1942-56; older pts. comprise an increasing proportion of stomach cancer cases. The ratio of male to female lung cancer was 5:1, with women more likely to have adenocarcinoma and men more likely to have squamous cell carcinoma. The relative rate of cervical cancer was higher among married, widowed, separated or divorced women, among Negroes, and among low-income groups. Prostate cancer comprised 11% of all male cancers reported. Leukemia pts. showed a bimodal age distribution, with a peak in the group under 15 and another in the group 65-74 yr.

- 64-953 LUNG CANCER IN FLUORSPAR MINING COMMUNITY. I. RADIATION, DUST, AND MORTALITY EXPERIENCE. (E.) De Villiers, A. J. (Dept. Natl. Health Welfare, Ottawa, Canada) and J. P. Windish. *Brit. J. Industr. Med.* 21(2):94-109, 1964.

While some airborne dust collections in 6 mines of the small fluorspar mining community of

St. Lawrence, Newfoundland, were above the threshold limit, no abnormal air fluoride levels were uncovered. On the contrary, underground workers were exposed to an av. potential alpha-energy/liter for radon-222 and radon daughters between 2.5-10 times the suggested working level of 1.3×10^5 Mev/liter of air. Of 119 deaths among employees and ex-employees from 1933-61, 43/119 were due to malignant neoplasms of all sites, of which 26/119 (age range 33-56 yr.; av. age 46.8 yr.) were due to cancer of the trachea, bronchi and lung. The latter were localized in the hilar region in all but 1 case; they were more frequent in the right than in the left lung. The av. period between the first underground exposure and death was 19.1 yr., with a range of 11.5-25 yr. Comparisons between mortality rates for St. Lawrence and Grand Bank, in the same region but with no fluorspar miners, reveal a death rate from lung cancer for the former 29 times that expected for the age group 20-64 yr. (See also CRA 2(5):#954, 1964.)

64-954 LUNG CANCER IN FLUORSPAR MINING COMMUNITY. II. PREVALENCE OF RESPIRATORY SYMPTOMS AND DISABILITY. (E.) Parsons, W. D. (Dept. Natl. Health Welfare, Ottawa, Canada), A. J. de Villiers, L. S. Bartlett and M. R. Becklake. *Brit. J. Industr. Med.* 21(2): 110-116, 1964.

As a follow-up to the preceding abstract, a survey of respiratory symptoms, lung function tests and chest radiography was conducted among 384 men (280 fluorspar mine employees and 94 residents of St. Lawrence and 10 volunteers from Grand Bank). The incidence of pneumoconiosis and chronic bronchitis was found to have no bearing on the high lung carcinoma rates among miners. The significantly greater number of heavy smokers among St. Lawrence miners (72.1% consumed more than 15 g of tobacco/day) suggests that this factor may be a potentiating or synergistic one with other carcinogens. The high level of radioactivity in the air still remains the main factor causing high lung carcinoma incidence among these fluorspar miners.

64-955 SYMPOSIUM ON THE CARCINOMAS OF THE MOUTH AND THROAT. (OROPHARYNGEAL CARCINOMA.) (E.) Menon, A. N. K. (Stanley Med. Coll. Hosp., Madras, India). *Antiseptic* 61(4):281-286, 1964.

Of 30,219 and 1,619 pts. with proved carcinomas at Tata Memorial Hospital, Bombay and the Stanley Hospital, Madras, resp., 14,162 (85% male; 15% female; 50% of cases between 40-60 yr. of age) and 642 (55% male; 45% female; 82% of cases between 40-70 yr. of age) were suffering from oropharyngeal carcinoma. Leukoplakia was noted in 32% and melanoplakia in 20% of the Tata Hospital oropharyngeal cases, while poor oral hygiene was noted in 42% and 90% of the oropharyngeal cancer pts. at Tata and Stanley Hospitals, resp.

In the Stanley Hospital series of pts. with carcinoma, the most frequent sites were: cheek, 57.6%; tongue, 13.3%; alveolus, 8.7%; palate, 6.1%; miscellaneous, 4.7%; tumors not confined to one site, 4.7%; all the lesions were squamous cell carcinoma, except for three undifferentiated carcinomas. There appears to be a correlation of oral carcinoma with poor oral hygiene, the smoking of Indian cigarettes (beedi), reversed smoking of cheroots, clay pipe smoking (lip cancer) and pan chewing; there was little correlation with race.

64-956 BILIARY AND HEPATIC CARCINOMAS IN BEARS AT THE SAN DIEGO ZOOLOGICAL GARDENS. (E.) Dorn, C. R. (Dept. Public Health, Berkeley, Cal.). *Nature (London)* 202:513-514, 1964.

The occurrence of biliary and hepatic carcinomas in 5 bears which were housed in the same grotto (among a total of 8 grottoes) at the San Diego Zoological Gardens, for the major part of their lives, is described. Histopathological diagnosis revealed that 2 (males; 1 *Ursus horribilis* and 1 *Melursus ursinus*) had bile duct carcinoma; 2 (female, both *M. ursinus*) had adenocarcinoma; and 1 (male, *M. ursinus*) had an adenocarcinoma of the biliary tract. Another grizzly (*U. horribilis*) was not affected. The sloth bears were placed in the grotto after a short period of vacancy when it was cleaned and disinfected. It is felt that since the affected bears were confined to the same environment for most of their lives, a common causation is probable.

64-957 SEVERAL ETIOLOGICAL ASPECTS OF PRIMARY LIVER CANCER IN THE ADULT. THE INCIDENCE OF CANCER IN PATIENTS WITH CIRRHOSIS AND HEMOCHROMATOSIS (50 OBSERVATIONS). (Fr.) Girard, M., M. Plauchu and J.-P. Revillard. *Arch. Mal. Appar. Dig.* 52(12):1230-1231, 1964.

The study of 50 pts. with primary liver cancer (34 males; av. age of 60 yr.; 16 females, av. age 59 yr.) revealed no hereditary, dietary or professional factors (except 1 wine-grower with arsenicalism) which could be associated with this disease. The only condition that frequently preceded liver cancer was cirrhosis (48%). Yet cirrhosis did not introduce a typical macroscopic or microscopic morphology which indicated the type of cancer that would develop (hepatoma, cholangioma or hepatocholangioma), but it unquestionably complicated the prognosis. In this region of Lyon, France, the frequency of cancer developing after cirrhosis was approx. 3%. Idiopathic primary hemochromatosis followed by the development of cancer was seen in 3 or 60 cases (this figure does not include cancer pts. with pigmented cirrhosis).

64-958 THE INCIDENCE OF Gm(a), Gm(b) AND Gm(x) FACTORS IN MALIGNANT HEMOPATHIES. (Fr.) Eyquem, A. (Pasteur Inst., Paris, France),

J. Dausset and L. Podliachouk. Bibl. Haemat. (19):726-730, 1964.

The incidence of Gm(a) factor was within normal range in 104 pts. with Hodgkin's disease (48.1%) and 65 pts. with myeloid leukemia (50.8%), but diminished in 92 pts. with acute leukemia (39.1%) and 66 pts. with lymphoid leukemia (25.8%). In addition, 23 pts. were found with Gm(a-b-x-) factor: 16 with lymphoid leukemia, 5 with acute leukemia and 2 with myeloid leukemia. (See also CRA 1(9-10):#1833, 1964.)

64-959 SERUM GROUPS Gm(a), Gm(b) AND Gm(x) IN CANCER PATIENTS. (Fr.) Lille, I. (Inst. Pasteur, Paris, France), L. Podliachouk, P. Gabay, A. Eyquem and R. T. Saracino. Bibl. Haemat. (19):722-725, 1964.

See CRA 1(9-10):#1833, 1964.

64-960 THREE CASES OF MALIGNANT TUMORS ORIGINATING IN CONCURRENCE WITH LOCAL BONE TUBERCULOSIS. (Pol.) Tylman, D. (Acad. Med., Warsaw) and T. Witwicki. Chir. Narzad. Ruchu Ortop. Pol. 29(3):373-376, 1964.

Knee joint tuberculosis in a 34-year-old male and in a 16-year-old male transformed into malignant synovioma and into osteosarcoma, resp., and tuberculosis of the lumbar spine in a 24-year-old male transformed into chondrosarcoma. These changes occurred 16, 6 and about 18 yr., resp., after start of the tubercular process. None had any previous X-ray therapy. All 3 pts. were then treated surgically, but died 24, 6, and 5 mo. later, resp.

64-961 THE CHANGING INCIDENCE OF CERVICAL CARCINOMA. (E.) Ruch, R. M. (Dept. Obstet. Gynec., Baptist Mem. Hosp., Memphis, Tenn.), C. Blake, A. Abou, M. Lado and W. A. Ruch, Jr. Am. J. Obstet. Gynec. 89(6):727-731, 1964.

The incidence of cervical carcinoma in Shelby County, Tennessee was reduced by 51% (from 39/100,000 to 19/100,000) between 1949 through 1961 as a consequence of cytological screening and consequent treatment of 75% of white women, age 20 or over. From 1953 to 1961, the death rate from cervical carcinoma decreased by 59% (from 22/100,000 to 9/100,000). In 1961, 20/25 cases diagnosed as invasive carcinoma had never had cervico-vaginal smears. Of these 25 cases, 67% were in Stage I, in contrast to 57% in the same stage in 1957 and 34% in 1952.

64-962 LUNG CANCER IN A RURAL ALPINE REGION FREE OF AIR POLLUTION. (Ger.) Gsell, O. (Clin. Med., U. Basel, Switzerland) and C. Jung. Deutsch. Med. Wschr. 89(19): 909-919, 1964.

In a detailed statistical study of the incidence of lung cancer in a Swiss alpine canton (Glarus) in which approx. 22% of the total population of approx. 40,000 worked in textile factories, but which was assumed to be relatively free of air pollution, the annual absolute incidence of male deaths due to lung cancer was 17 between 1941-50, 42 between 1951-60 (for women, 5 and 15, resp.). (Two counties bordering on Glarus were included in the tabulated data.) A total of 102 men dying of lung cancer between 1941-61 were evaluated in terms of tobacco consumption, a "cigarette unit" (CU) consisting of the amount of tobacco equivalent to that contained in a 1 g cigarette. The group was aged 36-90 (av., 61.5; median range, 46-74). Two were non-smokers; 4 consumed 10-19 CU/day; 33, 20-34 CU; 63, 35 or more CU. Among the 100 smokers, 27 smoked only cigars; 26, cigars and a pipe; 7, only a pipe; 22, only cigarettes; 18, cigarettes + a pipe or cigars. The mean age of death among pipe and cigar smokers was 64.9; among cigarette smokers, 57.0. Both lung cancer incidence and smoking habits are compared at length with those in other parts of Switzerland. The authors conclude that the relatively low incidence of lung cancer in Canton Glarus was not due to a relative absence of air pollution but to the fact that inhabitants of rural areas do not smoke as much as city dwellers. The data is construed as confirming a positive relationship between smoking (including cigar smoking) and the incidence of lung cancer. (The authors point out that "cigars", in this study, refers to the Swiss "Stumpfen" or Italian-type "stogies", and not to the types of cigar which are in common use elsewhere.)

64-963 FAMILIAL GASTRIC CANCER. (E.) Jones, E. G. (Dept. Anat., Otago Sch. Med., Dunedin, New Zealand). New Zeal. Med. J. 63(381): 287-296, 1964.

The study of a Maori family (who have lived in the same small area of Mount Maunganui peninsula for 100 yr.) revealed a preponderance of deaths and illnesses due to gastric cancer which was too high to be based on chance or racial predisposition. Of 167 kindred, there were 5 proven, 1 probable and several possible gastric cancers. Since the majority of those affected occurred in the present young generation, the author suggests that part of the family is at the confluent point of two distinct cancer trends: a polygenetic predisposition has been rather intensified and modified by intermarriage. However, no single dominant genetic factor can be traced, although most affected members belonged to blood group A.

64-964 CANCER INCIDENCE IN RELATION TO TRACE ELEMENTS IN SOILS, PLANTS AND DRINKING WATER. (E., Abstract) Davies, R. I. (Dept. Biochem., Bangor, University Coll. North Wales, England), P. Stocks and D. A. Jenkins. P. 442 in British Empire Cancer Campaign 1963. Part 2:

Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Chemical analysis of soils, plants and water has shown a statistical correlation between the occurrence of an excessively high ratio of available zinc to available copper in soils and the occurrence of stomach cancer in humans associated with the soils. Measurements of the zinc/copper ratio in 750 samples of soil from gardens in North Wales, Cheshire and two localities in Devonshire showed that in every one of 12 districts the av. logarithm of this ratio was higher in gardens at houses where a person had just died, after ten or more yr. of residence, of stomach cancer, than it was where a person had died similarly, but of a non-malignant disease; this effect was more pronounced for vegetable garden soils than for other soils.

64-965 REPORT OF THE CANCER RESEARCH UNIT OF MPIO CENTRAL HOSPITAL, BULAWAYO, SOUTHERN RHODESIA. (E., Abstract) Skinner, M. E. G., W. F. Ross and H. Mitchell. Pp. 550-551 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

A Cancer Research Unit, conducting an investigation into the incidence of all cancers in Africans and non-Africans for the Bulawayo urban area and districts from January 1, 1963 to the present, found the following were the most frequently registered tumors in Africans (number of cases, percentage of all registered cases): liver (primary; 65, 11%); cervix uteri (52, 8.8%); skin (excluding Kaposi; 47, 8.0%); bladder (45, 7.6%); esophagus (44, 7.5%); bronchus (37, 6.3%). The most frequently registered tumors in non-Africans were: skin (151, 4.7%); breast (27, 8.0%); bronchus (18, 5.3%); large bowel (17, 5.0%); cervix uteri (14, 4.1%).

64-966 RETINOBLASTOMAS. (E.) Gaisford, W. (Dept. Child Health, U. Manchester, England) and A. C. P. Campbell. Pp. 642-644 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

A survey of children in the Manchester Hospital Region affected by retinoblastoma from 1900-1959 revealed 151 proven cases, of which 101 are still alive. Whereas the male:female ratio was about equal among children presenting with the tumor under the age of one yr., there was a considerable excess of boys among those who presented between 1-3 yr. In all but two fatal cases, the tumor recurred within 3 yr. after removal of the eye; the orbit from which the eye had been enucleated was the most frequent site. Examination of the remaining eye of the survivors and their relatives produced five individuals in whom there was evidence that there had been retinoblastomas which

had regressed spontaneously. There was a suggestion that sex might have an influence on the tendency to regression. In the pts. with unilateral tumors, the distribution of ABO blood group types was approx. the same as in the general population while in those with bilateral tumors there was an excess of group A. There was no evidence of an inherited factor in the large majority of pts. It was estimated that where there is no antecedent family history of retinoblastoma, the chance of a survivor's passing on the tumor to succeeding generations lies between 20 and 50%. In view of this and the high survival rate, it was assumed that the number of pts. who inherited the disease would increase in future yr.

64-967 GASTROINTESTINAL PLASMACYTOMAS. A STUDY OF THREE CASES. (Fr.) Konuralp, H. Z. (2nd Clin. Surg., U. Istanbul, Turkey), O. Iskeçeli and S. Bekem. Lyon Chir. 59(6): 835-841, 1963.

Three case histories (2 men, 1 woman; age 35, 49 and 50 yr.) are presented of g.i. extramedullary plasmacytoma localized in the stomach, cecum and ileum. In a review of the literature (8 references) it is noted that the total number of g.i. plasmacytomas reported to date is 31, of which 7 were found in Turkey.

64-968 A DISCUSSION OF SURGICAL TREATMENT OF PULMONARY CANCER. (Sp.) Pintos Fuentes, R. and J. R. Fossemale. Rev. Esp. Tuberc. 32(343):489-496, 1963.

In a review of initially presenting symptoms, diagnostic procedures and findings, and progress of the disease among 108 pts. with cancers of the lung, the authors report evidence that the incidence of asymptomatic pulmonary cancer (as demonstrated by chest X-ray of the general population and/or of particular groups) is higher than generally supposed. In the general population, it is estimated to range from 4-6/100,000 persons; among those over 40 (both sexes), it is estimated to be approx. 129/100,000; among men over 40, it is estimated to be 270/100,000. (No references)

64-969 GARDNER'S SYNDROME. A FAMILY GROUP STUDY AND REVIEW. (E.) Weary, P. E. (Dept. Derm., U. Virginia Sch. Med., Charlottesville), A. Linthicum, E. P. Cawley, C. C. Coleman, Jr. and G. F. Graham. Arch. Derm. (Chicago) 90(1):20-30, 1964.

Both the case history of a 16-year-old girl with Gardner's syndrome as well as a genealogy containing the histories of 33 individuals in five generations give further evidence that Gardner's syndrome is a dominant hereditary disorder and the multiple polyposis which often occurs has significant malignant potential. All of the 10

family members who had died showed symptoms of Gardner's syndrome; 4 died of carcinoma and 1 of myeloid leukemia. Of the 23 living members, all had records of cysts, 3 underwent a colectomy, 4 had polyposis of the colon and 14 were not examined. In a review (53 references) of the 118 acceptable cases of Gardner's syndrome reported to date in the literature, the sex incidence was 67 males, 50 females and 1 unspecified; 2 pts. were Negro, the rest Caucasian; incidence of malignant alteration of polyps was 45% with only 1 case before the age of 20.

64-970 REPORT OF THE MEDICAL RESEARCH LABORATORY, NAIROBI, KENYA. (E., Abstract) Linsell, C. A. (Dept. Path., Med. Res. Lab., Nairobi, Kenya) and R. Martyn. Pp. 545-547 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

A comparison of cancer incidence (percentage) for the period 1957-1963 in Tanganyika (from the annual report of the Medical Laboratory, Dar-es-Salaam) and Kenya revealed the following: mouth, 2.1 and 0.4; nasopharynx, not stated and 2.3; esophagus, 0.3 and 3.9; stomach, 0.9 and 2.5; intestine, 0.7 and 2.5; liver and biliary duct, 3.0 and 5.2; nasal cavity and sinuses, 0.4 and 1.2; breast, 3.4 and 4.6; cervix uteri, 8.2 and 6.6; penis, 3.0 and 1.0; bladder, 2.6 and 1.0; skin (melanoma), 6.0 and 4.8; skin (squamous cell), 16.3 and 15.6; skin (basal cell), 1.4 and 0.8; connective tissue, 5.3 and 4.9; Kaposi's sarcoma, 4.7 and 2.4; reticulum cell sarcoma, 4.6 and 2.5; lymphosarcoma, 5.2 and 9.6; Hodgkin's disease, 2.1 and 2.5, resp. In liver and breast cancers, although incidences were similar, the male/female ratios were 5:1 and 1:12, resp., for Tanganyika and 3:1 and 1:7, resp., for Kenya. Some of the significant differences in incidence (oral and g.i. cancer) in the two countries are due to better diagnostic facilities in Kenya. The authors feel that the higher rate of cancer of the penis in Tanganyika is related to the uncircumcised status of many of the tribes there, and that Burkitt's sarcoma is a variant of lymphosarcoma and not a unique tumor with a specific etiology. (See also CRA 1(12):#2162; and ibid., #2204, 1964.)

64-971 THE CANCER REGISTRY, JAMAICA. (E.) Bras, G. and D. C. Watler. Pp. 552-554 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

In Jamaica, a total of 870 cancer pts. were registered in 1963: 346 were from country areas and 524 from Kingston and St. Andrew. This latter group of 524 was composed of 325 females (highest incidence between the ages of 35-75 yr.) and 199 males (highest incidence between 45-75 yr.). When the total number of cases between 1958-1963

were classified according to the site of the carcinoma and then compared with the expected number of each category as determined from a similar Danish population, the incidence of cancer of the esophagus, cervix, prostate, penis and skin was greater than predicted. The incidence of cancer of the lip, stomach, colon, testis and breast was notably lower than the statistical prediction.

64-972 AN AUTOPSY CASE OF ACUTE MYELOID LEUKEMIA IN WHICH THE ANTE-MORTEM ONSET COINCIDED WITH THE DEVELOPMENT OF CHRONIC LEUKEMIA IN THE PATIENT'S MOTHER. (Jap.) Donao, T. (Cent. Hosp. Soc. Insur., Japan) and H. Saito. Rinsho Ketsueki (Jap. J. Clin. Hemat.) 4(2):205, 1963.

A 34-year-old Oriental male developed acute myeloid leukemia about the same time that his 55-year-old Oriental mother developed chronic leukemia. The former was the eldest of five siblings. There was no other history of malignancy or hematopoietic disorder in the family.

64-973 ASBESTOSIS AND PULMONARY NEOPLASIAS. FURTHER CONTRIBUTION TO A CLINICAL CASE. (It.) Farina, S. (Inst. Spec. Path., U. Bologna, Italy) and G. Mazzanti. Lavoro Um. 15(6):276-281, 1963.

The authors discuss the possible carcinogenic properties of asbestos fibers and report the case of a 54-year-old man employed in the manufacture of insulation materials who died 2 1/2 years after the onset and diagnosis of pulmonary asbestosis. At the time of death the evidence indicated the development of pulmonary neoplasia.

64-974 SILICOSIS AND CANCER OF THE LUNG IN HOKKAIDO. SECOND REPORT: RELATIONSHIP BETWEEN FREE SILICON LEVELS AND CANCER OF THE LUNG. (Jap., Abstract) Takeda, K. (Dept. Path., Hokkaido U. Sch. Med., Japan), K. Aizawa, H. Kikuchi, T. Kodama, T. Miyashita and K. Hirai. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Japon.) 52:202-203, 1963.

Out of 46 Oriental pts. with silicosis reported in Hokkaido for the past 8 yr., 22 (44.7%) were complicated by malignant tumors: carcinoma of the lung, 8 (17.4%); carcinoma of the stomach 5 (10.8%); carcinoma of the liver, and others. There were also 17 benign tumors. Out of 88 pts. with carcinoma of the lung (excluding cases with silicosis of the lung) encountered in Hokkaido for the past 10 yr., 44 (50%) had silicosis of the hilar lymph nodes. For comparison, among 126 pts. (over age 41 yr.) with various lung lesions other than primary carcinoma of the lung, 38.9% had silicosis of the lung, 13.5% did not have silicosis of the lung, and 12.5% had metastatic carcinoma lesions in the lung. The incidence of silicosis of the hilar lymph nodes gradually

increased with age above 50 yr. among the pts. not having primary carcinoma of the lung, but remained consistently high under or above 40 yr. of age among the pts. having primary carcinoma of the lung, suggesting the presence of a close relationship between silicosis and carcinoma of the lung. In 5 lung cancer pts. with silicosis of the lung, the amount of free silicon av. 784 mg/100 g dry tissue in cancer lesions and an av. 671 mg in non-cancer lesions, as compared with an av. of 1026 mg in non-lung cancer pts. with silicosis of the lung. The authors stated that in 33 lung cancer pts. without silicosis of the lung, but with or without silicosis of the hilar lymph nodes, there was no significant difference in the amount of free silicon in cancer lesions as compared to non-cancer lesions.

- 64-975 PRECANCEROUS LESIONS OF THE LARYNX. (CLINICAL, STATISTICAL AND PATHOLOGICAL ANATOMICAL STUDY.) (It.) Bottura, M. (Ospedali civili riuniti di Venezia, Venice, Italy) and E. Forti. Gior. Veneto Sci. Med. 17(11/12): 433-455, 1963.

In a study of the relationship of laryngeal cancer to precancerous lesions, it was found that 28 of a total of 266 lesions (224 men; 42 women) developed into malignancies. Localizations (men, women) were as follow: chord, 149 and 20; false chord and ventricle, 41 and 9; vestibule, 18 and 6; epiglottis, 12 and 5; subglottis, 4 and 2. For men the age incidence was max. around 51-70 yr. (138 cases), and for women 41-60 yr. (29 cases). The incidence of malignant change in relation to probable cause and the structure affected was as follows: Tobacco + alcohol + voice strain, 14 chord and 1 false chord; hydrocarbons (refinery), 2 chord and 1 epiglottis; exposure to peroxides and ozonides, 1 vestibule; voice strain in overheated environment, 4 chord and 1 vestibule; glass blowing, 4 chord. Incidence of cases in relation to the time lapse observed between the finding of the precancerous lesion and the onset of malignancy was, for the time intervals 1-5 mo., 6-12 mo., 1, 3 and 5 yr., resp.-- tobacco + alcohol + voice strain: 0, 7, 5, 1, 2; hydrocarbons: 0, 2, 1, 0, 0; peroxides and ozonides: 0, 1, 0, 0, 0; voice strain in overheated environment: 4, 1, 2, 0, 0; voice strain: 0, 2, 1, 1, 0. The 28 cases of malignant degeneration are reported in detail.

- 64-976 INDIRECT FLUOROSCOPIC METHOD IN MASS EXAMINATION OF THE STOMACH. (Jap.) Ariga, K. (Dept. Int. Med., Nihon U., Japan), K. Takahashi, Y. Goto and R. Kurihara. Rinsho Hoshasen (Clin. Radiography) 8(9):655-671, 1963.

In a community mass examination of a total of 13,844 Oriental individuals for carcinoma of the stomach with the use of various screening methods, the authors detected 78 cases (0.56%) of carcinoma of the stomach. The initial major screening

method used was indirect fluoroscopic examination. No details are given as to the method of selection of the individuals subjected to this mass examination.

- 64-977 A MASS SCREENING EXAMINATION FOR LUNG CANCER. (Jap.) Sakuma, T. (Div. Labor, Bur. Gen. Affairs, Tokyo Metropol. Gov.), K. Kakita, O. Oohigashi, Y. Hayada, M. Ozaki, G. Hayashi and T. Yoshida. Nippon Kyobu Rinsho (Jap. J. Chest Dis.) 22(11):746-757, 1963.

A mass screening examination for lung cancer carried out on a total of 527,020 Tokyo City Office employees, ages 18-70, between 1953-1962, detected 62 cases of lung carcinoma. This represents an incidence of lung carcinoma (per 100,000) of 11.76 for those between 18 and 70 yr. of age, or a rate of 30.10 for subjects more than 40 yr. of age. As for age distribution, none occurred below 39; the rate was 6.7 for those between 40-49 yr.; 31.5 for those between 50-59 yr.; and 89.9 for those above 60 yr. In subjects 18-70, the rate for males and females was 14.2 and 4.0, resp., and 33.8 and 13.7, resp., for those more than 40 yr. of age. The primary screening method was the use of the routine chest roentgenography.

- 64-978 STATISTICAL STUDY OF MORTALITY RATES OF PATIENTS WITH CARCINOMA IN TERMS OF AGE AND SEX. (Jap.) Segi, M. (Dept. Public Hygiene, Tohoku U. Sch. Med., Japan), Y. Narai and K. Segi. Shindan To Chiryo (Diag. Ther.) 52(1):160-163, 1964.

This paper deals with the mortality rates of pts. with carcinomas of the esophagus, stomach, or lung. Statistical data were analyzed in terms of age and sex and compared with corresponding statistics in England and the U. S.

- 64-979 COMPARATIVE STUDY OF MORBIDITY AND MORTALITY DATA OF CANCER IN SEVILLE. (Sp.) Stiefel, E., J. Parra, P. Solaeche, J. Lashera and T. Cámara. Arch. Cancerol. 2(1): 39-43, 1963.

A study of the incidence of malignant tumors seen at the Centro de Cancerologia of Seville for the period 1955-1962 showed that there was no marked difference of the relative frequencies compared to 1962. The most frequent sites seen during the 7-year-period were: mammary (132), skin (128), uterus (98), lung (62), larynx (59), lips (56), stomach (34), and tongue (31). These cancers plus those of the mucous membranes and female genital tract constitute 82% of all cases seen.

- 64-980 LUNG CANCER AND MONTH OF BIRTH. (E.) MacSween, R. N. M. (U. Dept. Path., Western Infirmary, Glasgow, W. 1, Scotland) and S. E. P. Miller. Lancet 1:767-768, 1964.

A statistical survey comparing the mo. of birth in 200 cases of lung cancer which came to necropsy from 1953-1962 with the mo. of birth in 200 pts. examined post-mortem in 1962 (regardless of sex and diagnosis, but excluding lung cancer) failed to show any significant results. Nor were significant results obtained in a survey of seasonal occurrence in the same groups of pts. These results fail to support Dijkstra's original observation. A significant seasonal variation was found for oat-cell carcinoma, however, when histologic types (squamous cell carcinoma, adenocarcinoma, oat-cell carcinoma and miscellaneous) were compared: 11, 6, 10 and 13, resp., for February-April; 14, 6, 24 and 14, resp., for May-July; 14, 8, 13 and 13, resp., for August-October; 16, 11, 9 and 18, resp., for November-January. A significant seasonal variation in the mo. of death of pts. with lung cancer was also found: 42 for February-April; 50 for May-July; 71 for August-October; 37 for November-January. (See also CRA 2(1):#152, 1964.)

64-981 LUNG CANCER AND MONTH OF DEATH. (E.)
Record, R. G. Lancet 1:934-935, 1964.

In connection with the recently reported point (see CRA 2(5):#980, 1964) that lung-cancer deaths in Glasgow are more likely in the mo. August-October, data from the Registrar General for Scotland (1953-1962) showed a later peak of excess deaths (September-December) with a lesser degree of variation (+2.8-+7.2%). There were excess deaths in February (+4.6%) followed by March with the lowest rate (-6.8%). Examination of data for 1960-1962 from the Registrar General for England and Wales reveals excess thoracic cancer deaths in each mo. from September to February; the max. was in November (7.2%), the lowest figure was in June when deaths were 4.9% below expectation. This may reflect possibly a combination of factors (infection, air pollution) which may influence the final stages of the disease.

64-982 CLINICO-STATISTICAL OBSERVATIONS OF
TUMORS OF THE BRAIN IN INFANCY AND
CHILDHOOD DURING A RECENT 10-YEAR PERIOD. (Jap.)

Shingu, T. (Dept. Geriat., Kurume U. Sch. Med., Japan), K. Nomasa, T. Nishimon and M. Kotaki. Kurume Igakkai Zasshi (J. Kurume Med. Assn.) 27(1):61-63, 1964.

Among 15,749 pediatric outpatients observed in Kurume Univ. Hospital during the period 1952-1961, 22 brain tumors (0.14%) were diagnosed. Incidence was not related to sex or age. The clinical aspects were also reviewed (5 references).

64-983 CANCER OF THE DIGESTIVE TRACT IN
COLOMBIA. STATISTICS OF THE NATIONAL
CANCER REGISTRY FOR 1961. (Sp.) Gaitan-Yanguas, N. (Natl. Inst. Cancerology, Bogotá, Colombia). Unidia 10(2):63-69, 1963.

In a survey conducted in 1961 for the National Cancer Registry of Colombia, a total of 6,077 cancer cases (90% with histologic confirmation; rate 42/100,000 population) showed the following distribution: female genital tract 25.2%; digestive tract 24.3%; skin and adnexa 21.3%; breast 7.8%; lymphoid-hematopoietic system 5.9%; respiratory tract 4.3%; male genital tract 3.1%; urinary tract 2.1%; skeletomuscular system 1.9%; <1% each for endocrine, eye and orbit, soft tissue, nervous and other systems. Cancer of the digestive tract was found to occupy second place both in incidence and in death rate and its distribution (based on 1,479 cases) was as follows: stomach 546 cases, mouth 264, esophagus 174, colon and rectum 150, liver 63, biliary tract 48, tonsils 40, salivary glands 39, pancreas 28, pharynx 21, small intestine 15, peritoneum 14, anus 8, unspecified 26, metastatic 43. Gastric cancer was found to increase by 15 cases in 10 yr. and was most frequent in the age group 50-69 yr. (309 cases), followed by 103 cases for ages 40-49, 51 cases for ages 30-39 and 42 cases for ages 70-79. Incidence of esophageal cancer was highest (109 cases) for age group 50-69 yr., followed by an incidence of 24 cases for ages 70-79 and 23 cases for ages 40-49. Cancer of the stomach represented 9% of all cancers and showed a male/female ratio of 3:2 (2.4:1 for age group 50-59 yr. alone); the male/female ratio for cancer of the esophagus was approx. 2:1.

See also abstract nos.: 806,813,822,873

MISCELLANEOUS

- 64-984 CHROMOSOME ANALYSIS OF CANCER CELLS AND OF IN VITRO IRRADIATED BONE MARROW AND BLOOD CELLS. (Fr.) De Grouchy, J. (Natl. Inst. Hyg., Paris), G. Vallée, C. Nava and M. Lamy. Ann. Genet. (Paris) 6(1):9-20, 1963.

Chromosome analysis of cells obtained from malignant effusions secondary to an ovarian cyst, an ovarian carcinoma and a breast adenocarcinoma showed the following abnormalities: an acrocentric chromosome (designated K1, same size as group 4-5) in all cells of the cyst and in 30% of those from the ovarian carcinoma; a larger subtelocentric chromosome (K2) in all cells from the breast cancer. The distribution of the chromosome numbers in the three cancers was paradiplod at 45, 48 and 40, resp., and hypotetraploid at 88-90 and 52-62 in the ovarian cancer. In vitro irradiation (100-300 r) of bone marrow cells and peripheral blood leukocytes from individuals of normal karyotype showed fewer chromosome rearrangements in bone marrow cells than in peripheral blood leukocytes. The results are discussed in reference to the chromosome theory of carcinogenesis; it is suggested that chromosome rearrangement, serving as a common pathway for various carcinogenic factors (X-rays, virus, chemical carcinogens), may be considered an ultimate cause of carcinogenesis.

- 64-985 CANCER ARISING IN SCARS OF OLD BURNS AND IN CHRONIC OSTEOMYELITIS, ULCERS, AND DRAINAGE SITES. (E.) Engler, H. S. (Dept. Surg., Coll. Med. Georgia, Augusta), A. Fernandez, F. E. Bliven and W. H. Moretz. Surgery 55(5): 654-664, 1964.

In 9/20 pts. with Marjolin's ulcer admitted to Talmadge Memorial Hospital over the past 6.5 yr. (5 males, 4 females; av. age 50 yr.; av. latent period 26.3 yr.), there was an association with old burn scars (8 thermal, 1 chemical), of which 8/9 were squamous cell carcinomas and 1 was a basal cell carcinoma. All of the 5 neoplasms arising in pts. with chronic osteomyelitis following a fracture were squamous cell carcinomas (3 males, 2 females; av. age 17 yr.; av. latent period 38 yr.). One adenocarcinoma and 2 squamous cell carcinomas developed in perineal drainage sites (2 males, 1 female; av. age 59 yr.; av. latent period 12 yr.). All 3 carcinomas (in 1 male and 2 female pts.; av. age 72 yr.; av. latent period 19 yr.) in pts. with chronic ulcer of the legs were squamous cell carcinomas. The authors review similar incidences found in the literature (27 references), the metastasizing capacities of these cancers, and the result of radium, X-ray and surgical treatment. Of the 20 pts. reported here, 3 had regional lymph node metastases and 2 showed more distant spread of the neoplasm.

- 64-986 STUDIES OF THE ANTIGENS OF HUMAN TUMORS. I. DEMONSTRATION OF A

SOLUBLE SPECIFIC ANTIGEN IN HeLa CELLS AND SOME HUMAN TUMORS. (E.) McKenna, J. M. (Harrison Dept. Surg. Res., U. Pennsylvania Sch. Med., Philadelphia), R. P. Sanderson and W. S. Blakemore. Cancer Res. 24(4):754-762, 1964.

The presence of a soluble specific antigen serologically identical with HeLa(G) antigen was shown in 31% of human malignancies. According to cell type diagnosis, the antigen has been found in 13/33 adenocarcinomas, 3/6 undifferentiated carcinomas, 3/7 squamous cell carcinomas, 5/12 melanomas, 1 leiomyosarcoma, 3/6 hypernephroid carcinomas, 1 neuroblastoma, 1/2 pheochromocytomas and 1/3 lymphosarcomas. No correlation seems to exist between the degree of malignancy of the diseased tissue and the presence or absence of the antigen. The antigen was not found in 27 normal tissues nor in 10 benign tumors of the uterus.

- 64-987 MARKER CHROMOSOMES OF EHRlich ASCITES CARCINOMA. (E.) Hsu, L.-C. (Shanghai Tumor Res. Inst., China), H.-S. Yu, W.-S. Ch'i and C.-Y. Ts'ao. Chin. Med. J. 83(1):32-38, 1964.

When hyperdiploid Ehrlich ascites carcinoma cells (ELD; transplanted serially in Swiss mice for 5 yr.), inj. i.p. (0.2 ml ascitic fluid) into adult male mice (15-20 g; strain not stated), were extracted on day 3 after transplantation (when they showed a high mitotic rate), histologic examination revealed three types of marker chromosomes: metacentric, telocentric with secondary constriction, and minute. The morphological characteristics and frequency of these marker chromosomes are described.

- 64-988 ACQUISITION OF HEIGHTENED RESISTANCE AND SUSCEPTIBILITY TO SPONTANEOUS MOUSE MAMMARY CARCINOMAS IN THE ORIGINAL HOST. (E.) Weiss, D. W. (Dept. Zool., U. California, Berkeley), L. J. Faulkin, Jr. and K. B. De Ome. Cancer Res. 24(4):732-741, 1964.

Transplanted C3H/f/Crgl nodule outgrowths produced spontaneous mammary carcinomas which were removed and retransplanted into their original C3H/Crgl/2 hosts and into isologous, tumor-free mice. Some from each of these series were treated with killed tumor cells and/or with immunological activators (tubercle bacillus fraction, DNA digest, bacterial endotoxins). Tumors grew in all isologous controls. Tumor growth was either appreciably retarded or facilitated in a majority of the original tumor-bearing animals as compared to their isologous controls. Several original hosts failed entirely to support transplant growth, and in more than 50% of the remaining experiments the original animal ranked either first or last in order of resistance to the transplants. The lymph nodes draining the site of tumor implantation showed exaggerated lymphoid hyperplasia,

suggesting active immunological response, in original animals exhibiting either resistance or enhancement. Heightened tumor resistance was also seen in autochthonous hosts when tumors arising spontaneously in multiparous breeding females were used.

64-989 SERUM LIPOPROTEINS AND HUMAN NEOPLASTIC DISEASE. (E.) Barclay, M. (Sloan-Kettering Inst. Cancer Res., New York), G. C. Escher, R. J. Kaufman, O. Terebus-Kekish, E. M. Greene and V. P. Skipski. Clin. Chim. Acta 10(1):39-47, 1964.

Comparative serum lipoprotein studies showed higher amounts of S_f20-100 and S_f0-100 in 9 women with advanced breast cancer (av. age 41 yr.) (30 mg/100 ml and 40 mg/100 ml, resp.) than in 20 normal women (av. age 32 yr.) (3-8 mg/100 ml and 5-21 mg/100 ml, resp.). All lipoproteins with densities < 1.0635 g/ml were not elevated in cancer pts. Of the several high-density lipoproteins measured, only those floating at soln. density of 1.125 g/ml (S_f0-4 or HDL₂) were markedly lower in cancer pts.

64-990 INTERRELATIONSHIP BETWEEN VITAMIN B₁₂ AND GASTROMUCOPROTEIN IN LEUKEMIA. (Rus.) Ponomareva, E. D. (Dept. Ther., Inst. Post-Grad. Med., Moscow). Ter. Arkh. 36(2): 2-80, 1964.

The vitamin B₁₂ content was studied in 20 leukemia pts. In both acute and chronic myeloid pts., while there were definite fluctuations and non-significant decrease in secretion of gastric mucoprotein, this was not correlated with increased vitamin B₁₂; there also was no correlation with changes in gastric acidity, hyperchromia and with the presence of erythroblasts in the blood. The livers of pts. who died of leukemia showed increased liver vitamin B₁₂, compared to controls. This might indirectly indicate inefficient utilization of the vitamin by the erythroblasts of the bone marrow. Two cases are reported in some detail.

64-991 BIOLOGICALLY ACTIVE DNA FROM CANINE LYMPHOMA CELLS. (E.) Prier, J. E. (Vet. Med., U. Pennsylvania, Philadelphia), D. F. Cain and J. Chambers. Nature (London) 202:611-613, 1964.

Cell-free DNA (0.2 ml/tube), obtained from lymph nodes and spleens of dogs with lymphoma, was added to cell cultures of dog kidney, cytological effects, consisting of increase in cell size (particularly of the cytoplasm) and a decrease in the total number of cells, were seen after 48 hr. Pre-treatment with DNase (50 µg/ml of DNA preparation; 30 min. at 25°C) destroyed the ability to produce cytologic effects. RNase was not effective in eliminating the cytologic effects.

Treatment with isolated DNA obtained from the spleens of lymphoma animals caused an increased sensitivity to cysteine repression in recipient (primary canine kidney) cells. Preparations obtained from lymph nodes of lymphoma animals were not as active.

64-992 CARCINOSARCOMA OF THE LIVER. (Rus.) Bialik, V. V. (Kiev A. A. Bogomolets Med. Inst. [Order Red. Banner Labour], USSR). Ark. Pat. 26(6):76-79, 1964.

A case is presented of a man (age 56) with a carcinosarcoma which developed in a cirrhotic liver which showed transitions from nodular hyperplasia and adenomas to hepatocellular carcinoma. There also was malignant change of the connective tissue with development of a typical spindle cell sarcoma.

64-993 A HISTOGENIC STUDY OF CHONDROBLASTOMA. (E.) Welsh, R. A. (Dept. Path., Louisiana State U. Sch. Med., New Orleans) and A. T. Meyer. Cancer 17(5):578-589, 1964.

Cells from 2 cases of chondroblastoma were studied by electron microscopy and compared with other chondroid tissues--fetal cartilage, chondrosarcoma and tissue culture of normal human cartilage. It was revealed that there was no similarity to fetal cartilage or chondrosarcoma cells. However, chondroblastoma cells strongly resembled normal human epiphyseal cartilage cells growing in the tissue culture. The hypothesis is offered that the chondroblastoma is a true neoplasm that arises as a reaction of normal cartilage cells to an altered local environment rather than to an intrinsic alteration of the cartilage cells per se.

64-994 MULTIPLE CHROMOSOME ABERRATIONS IN DOWN'S SYNDROME ASSOCIATED WITH TWINNING AND ACUTE GRANULOCYTIC LEUKEMIA. (E.) Rowley, J. D. (Argonne Cancer Res. Hosp., Chicago, Ill.). Lancet 1:664-665, 1964.

In a discussion of the conclusion reported by K. A. Kiossoglou et al. from the case history of a male child pt., namely, that genes located on the short arm of the X chromosome are not necessary for cell survival, the author suggests the need for further verification of the presumptive X-isochromosome, since the absence of late-labeling chromosome in the child would not be evidence for or against the existence of an iso-X-chromosome. Suggested additional studies of this child should include karyotyping of cells from the skin and other tissues; examination of cells from buccal mucosa and skin culture for sex chromatin; a detailed description of the physical examination of the child; a study of the presence or absence of sex-linked genes; a determination of the level of X-linked enzymes (like G6PD). Positive results would establish the location of these genes on the long arm of the X chromosome.

- 64-995 DISTRIBUTION OF METASTASES OF WALKER 256 IN RELATION TO THE ROUTE OF INOCULATION. (Pol.) Costachel, O. (Inst. Oncol., Bucharest) and I. Popp. Nowotwory 14(2):89-91, 1964.

Walker 256 tumor (5×10^6 cells) was inoc. into 122 male and 90 female WAG white rats by various routes. The incidence of metastases to lungs, liver, kidney, and adrenal, resp., was: with s.c. inoc., 3/21, 0/21, 0/21, 0/21 in males and 3/22, 1/22, 0/22, 0/22 in females; with i.v. inoc., 14/26, 0/26, 0/26, 0/26 in males and 12/25, 2/25, 1/25, 0/25 in females; with intramedullary (tibial bone marrow) inoc., 6/26, 0/26, 2/26, 0/26 in males and 8/23, 1/23, 6/23, 0/23 in females; with inoc. into the orbital venous plexus, 4/49, 1/49, 0/49, 0/49 in males and 4/20, 2/20, 0/20, 0/20 in females. Thus the renal metastases appeared almost exclusively after the intramedullary admin. and were more frequent in females than in males.

- 64-996 MALIGNANT CHANGE IN FIBROUS DYSPLASIA. REPORT OF A CASE. (E.) Riddell, D. M. (London Hosp., England). J. Bone Joint Surg. (Brit.) 46-B(2):251-255, 1964.

A brief review of the literature (17 references) on malignant change occurring in fibrous dysplasia is given along with an additional case with polyostotic fibrous dysplasia. In this case, biopsy revealed a pleomorphic spindle and giant-cell sarcoma with a high mitosis rate in an area of fibrous dysplasia.

- 64-997 MODIFICATION OF THE MITOTIC INDEX OF SARCOMA J DURING ITS EVOLUTION AS AN ANIMAL TRANSPLANT. (Fr.) Hublet, C. (Dept. Path. Anat., U. Liege, Belgium). C.R. Soc. Biol. 157(11):2101-2104, 1963.

Transplants (s.c.) of Sarcoma J (see CRA 2(2): #324, 1964) in normal female C57BL, immunized C57BL and hybrid (C57BL x R3A)F₁ mice, as well as i.m. transplants in normal C57BL mice, all showed an increasing mitotic index 15 days after-ward. The rate of increase of this index paralleled the rate of tumor growth. In C57BL mice which received s.c. transplants, some tumors began to regress at 17-20 days and, concomitantly, their mitotic index decreased. This diminished mitotic activity appears to be secondary to host immunization. However, other factors must be involved (and are currently being investigated), since mice previously immunized before receiving the transplant (a situation where tumors always eventually regress) showed the highest mitotic index at day 10.

- 64-998 MORPHOGENETIC STUDIES OF A TUMOR FORMING HYBRID IN NICOTIANA. (E., Abstract) Ahuja, M. R. (Inst. Cancer Res., Philadelphia, Pa.) and G. L. Hagen. Genetics 50(2):231, 1964.

Isolated tumor-bearing lines (having approx. 40% transmission of tumor trait) carrying an alien longiflora chromosome or its fragment on a 4n Nicotiana debneyi-tabacum background were investigated to find their nutritional requirements and to detect any differences in the type of differentiation in tumor and non-tumor plants in response to a particular medium. It was found that modified Hildebrandt's inorganic medium supported the growth of tumor hybrid pith tissue, but not that of non-tumor plants. Leaf or root response of tumorous or non-tumorous lines was found to depend on the presence or lack of coconut milk in the modified medium. Culturing the tumorous and non-tumorous tissues with varying conc. of kinetin (0.01-10 mg/l) indicated that at increased kinetin conc., non-tumor plants form shoots and not roots.

- 64-999 WALDENSTROEM'S MACROGLOBULINEMIA. DESCRIPTION OF AN ATYPICAL CASE.

(Pol.) Rogoz, J. (Clin. Int. Dis., Acad. Med., Katowice, Poland). Pol. Tyg. Lek. 19(22):840-842, 1964.

A 48-year-old man with reticulosis in the final stage of transformation into lymphosarcoma developed Waldenstroem's syndrome, but without macroglobulinemia. Despite attempts at treatment the pt. died soon afterwards.

- 64-1000 INCIDENCE OF TUMOURS IN BACK-CROSS MICE. (E., Abstract) Head, M. A. P. 533 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

C3Hf Female breeder mice had a higher incidence of mammary tumors (25.9%) than RIIIf breeders (2.6%). A 12% tumor incidence was noted in the hybrid C3Hf x RIIIf mice; however, when the female hybrid was mated with an RIIIf male, tumor incidence in the female progeny equalled that of the C3Hf strain. In male progeny the incidence of liver tumors was as high in the backcross mice as in C3Hf males (29.8%), much higher than in the RIIIf strain (8.8%) to which it was backcrossed; in the hybrid the incidence was 96.3%.

- 64-1001 COMPARATIVE STUDIES ON TWO ISOGENIC CELL LINES OF AUTOLOGOUS ORIGIN, ONE OF WHICH WAS TUMORIGENIC. (It.) Cassingena, R. (Dept. Microbiol., Superiore di Sanita Inst., Rome), R. Zito, V. Miggiano and P. Merucci. Rendic. Ist. Sup. Sanit. 26(8-9):727-751, 1963.

Further investigation (see CRA 1(5):#1012, 1963) of cell lines PG (non-tumorigenic) and PT (tumorigenic) have shown that PG did not develop tumorigenic activity even after 71 passages in vitro and that PT showed a reduction in tumorigenic activity between in vitro passages 60-117 but no change in latent period. A PTa1 line, developed from a PTa tumor of 19 days, retained 100%

umorigenic activity up to passage 65 and showed shorter latent periods than either PTa or PTb lines. PT cell lines and their derivatives (PTa and PTb) all showed similar fibroblast structures and more rapid growth curves than PG cell lines. Ta, PTb and PTaTl tumors proved 100% transferable when inoc. s.c. or i.m. into C57BL mice, had av. latent periods of 6.5 days and caused death in all animals within 1 mo. Primary PTa, PTb and TaTl tumors showed essentially the same structure (polymorphous cell sarcoma with prevalence of spindle cells), regardless of mouse strain used. Karyotype studies showed cell lines PG, PTa, PTb, etc., to be heteroploid; PTa, PTaTl and TaTlO cell lines showed stem-line numbers of 40; metacentric chromosomes were present in all cell lines, but not in all cells. PTaTlO showed marked reduction in the number of metacentric chromosomes; an extra long telocentric chromosome as seen in cell lines PT (64-103 passage), PTa, TaTl and PTaTlO. Glycolytic quotients were high for PG but higher in PTa, low in PTb and lower than PG in PTaTl.

64-1002 AUTOIMMUNITY AND CANCER, WITH SPECIAL REFERENCE TO SENILITY. HISTOLOGIC STUDIES. (It.) Sirtori, C. (Natl. Inst. Study Rare Tumors, Milan, Italy). Minerva Med. 55(7): 183-184, 1964.

The author reviews examples in the literature of spontaneous regression of such tumors as the neuroblastoma (3/30 cases personally observed), hypernephroma, melanoblastoma and chorionepithelioma of the uterus (1 personal observation) and analyzes various explanatory hypotheses. Among the hypotheses considered are: bioregulation (disappearance of aggregates of sympathetic tissue in early life) for neuroblastomas, hormone dependence for melanoblastomas, interruption of food supply for hypernephromas, and true immunization (incompatibility between chorionepithelious tissue of mother and fetus) for the chorionepithelioma. The following histologic patterns were found to characterize the immune state: lymphocytic reaction, lymphocytic reaction with germinal centers, necrosis, plasma-cellular reaction and appearance of giant cells similar to those found in the foreign body granuloma.

64-1003 STUDIES ON THE MECHANISM OF ISOANTIGENIC VARIANT FORMATION IN HETEROZYGOUS MOUSE TUMORS. III. BEHAVIOR OF H-2 ANTIGENS D AND K WHEN LOCATED IN THE TRANS POSITION. (E.) Klein, E. (Karolinska Inst. Sch. Med., Stockholm, Sweden) and G. Klein. J. Nat. Cancer Inst. 33(3):569-578, 1964.

The determinants of antigens D and K are located on 2 different homologous chromosomes (trans position) in tumors of (DBA/2 x C3H)F1 hybrid mice. Antigen D is derived from the H-2^d complex of the DBA/2 strain and K from the H-2^k complex of strain

C3H. Unlike that seen for the cis position, D-K+ variants were readily obtained. It is postulated that the formation of isoantigenic variants has a chromosomal mechanism, rather than representing either deletion or somatic crossing over.

64-1004 PULMONARY SARCOMA ARISING FROM A MALFORMED CONGENITAL CYSTIC PNEUMONOPATHY. (It.) Lucchesi, M. (Tubercul. Clin., U. Rome, Italy), G. Storniello and G. Pallotta. Riv. Tuberc. 11(6):411-431, 1963.

The authors describe the clinical course, radiologic findings and histologic characteristics of a fibro-chondro-myxosarcoma which developed in a 49-year-old man from a bronchogenic intraparenchymal cyst. A review (60 references) is included of all cases of pulmonary sarcoma reported in the literature during the past 20 yr., along with a discussion of the various histogenetic interpretations of these neoplasms.

64-1005 INDUCED TUMOUR RESISTANCE IN RATS. (E.) Buttle, G. A. H. (Dept. Pharmacol., U. London), J. Eperon and D. N. Menzies. Lancet 2:12-14, 1964.

Weanling rats (ARC "WAG") treated with cortisone-acetate suspension (66 mg/kg every 48 hr. x 4, i.m.) supported the growth of human sarcoma HS1 (0.5 ml of 40-50% cell suspension, i.m.), but in some cases tumor regression occurred. Seven days before challenging with the tumor and cortisone, inj. of 0.5 ml of 50% suspension of the following human cancer tissues produced varying degrees of tumor growth inhibition: breast carcinoma none; fibrosarcoma 46%; carcinomas of the bronchus 50%, liver 60% and rectum 82%; melanotic sarcoma 91-100%; synovial sarcoma 95%; and chondroma 97%. Inhibition was also caused by human normal cells: adult muscle 37%, placenta 74%, fetal muscle 79%, and fetal spleen 96%. Adult serum and spleen cells did not inhibit growth. Passive immunity was induced by human serum taken at the time of abortion, but not by serum of pts. with a history of repeated abortion during a subsequent pregnancy. When another group of rats received rat embryonic tissue or Walker tumor cells as an antigen source, the results were inconclusive. With mice, when an iron-dextran induced mouse sarcoma was used as the challenge, prior inj. with embryonic mouse liver or placenta increased resistance to the growth of the tumor. Mouse experiments, using the Crocker tumor as a challenge, proved negative.

64-1006 SUBDIPOLOID STEM LINE DEVELOPMENT. (E., Abstract) Talukdar, C. P. 115 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

A spontaneously occurring hepatoma in a DBA/2

mouse was composed of cells with 40 acrocentric chromosomes; after the tumor was transplanted to (DBA/2 x C57Bl)F1 hybrid mice, more than 50% of the neoplastic cells contained 38 chromosomes. This subdiploid stem-line remained stable up to the 18th transplant generation; in addition, 13% of the cells had extremely small chromosomes and 3-6% had large telocentric marker chromosomes.

- 64-1007 CHROMOSOME CONSTITUTION OF PRIMARY AND TRANSPLANTED LEUKAEMIA IN C58BL MICE. (E., Abstract) Talukdar, C. P. 115 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

Cells in the hematopoietic tissues of the primary leukemias studied showed a tendency toward an increased chromosome number during successive transplant generations. The normal number of 40 was seen in 80-91% in the original cells, whereas, by the fourth passage, 46% of the spleen cells in the leukemic animal had 41 chromosomes.

- 64-1008 MONORCHIA WITH SEMINOMA IN A CRYPTORCHID. AN UNUSUAL CASE OF TUMOR OF TESTIS. (E.) Sahi, R. P. (Dept. Surg., King George's Coll. Med., Lucknow, India) and R. V. Singh. Brit. J. Urol. 36(2):222-224, 1964.

A rare case is described of a 25-year-old pt. with a seminoma of the cryptorchid right testicle. At operation there was no evidence of the left testicle.

- 64-1009 STUDIES OF GLIOMA GROWTH IN MICE. II. IMMUNITY AFTER EXCISION. (E.) Wilkins, R. H. (Div. Neurosurg., Duke U. Med. Ctr., Durham, N.C.) and A. S. Ketcham. Arch. Neurol. 9(6):671-676, 1963.

The i.m. or intracerebral inoc. of gliomas 261, 26 and Z in C57Bl/6JN female mice which had previously been inj. i.m. with the tumors into the thighs and which had in turn been removed by amputation (9 days after inoc.) resulted in a significantly lower incidence of tumor takes in immunized animals than in controls. The only exception was seen with glioma 26 where immunized animals challenged i.m. developed as many tumors (100%) as did the unimmunized controls. The relative rates of tumor take with the other tumors were (immunized, controls): glioma 261--i.m. 0/20-8/20, intracerebrally 8/20-19/19; glioma 26--i.m. 20/20-20/20, intracerebral 1/19-17/18;

glioma Z--i.m. 11/19-20/20, intracerebrally 0/18-20/20. When 138 immunized mice were challenged s.c. 65 days after the immunizing inoc. (54 days after amputation), 36 developed small tumors within 2 wk. but all but 6 regressed and these showed indication of necrosis which was not seen in the 30 controls which showed 100% tumor takes. A certain degree of cross immunity could be shown, with glioma Z giving the highest protection.

- 64-1010 THE RELATION OF EMBRYOLOGICAL CONFIGURATION TO BASAL CELL CARCINOMA OF THE FACE. (Jap., Abstract) Miki, Y. (Osaka U., Japan). Nippon Hifuka Gakkai Zasshi (Jap. J. Derm.) 73(8):558, 1963.

A careful examination of 41 cases of basal cell carcinoma of the face revealed that the sites of carcinoma were situated on certain lines. These lines were found to correspond to facial grooves which appear during embryonic development. The author feels that burial of part of the germinative layer or some change in the cutis vera during embryonic development, coupled with some later external factor, may lead to the development of basal cell carcinoma.

- 64-1011 SUBCUTANEOUS TUMOR FORMATION BY SPARGANUM MANSONI IN MAN. (Jap.) Yoshino, T. (Dept. Surg., Niyodo Hosp., Ino, Kochi, Japan) and H. Takahashi. Nippon Geka Hokan (Arch. Jap. Chir.) 33(1):145-147, 1964.

A case of indolent tumors measuring approx. 1.0 cm in diameter in the s.c. tissue of the left thigh and left lower abdominal wall in a 36-year-old Oriental male was found to be due to Sparganum mansoni. The most probable source of infection was considered the ingestion of water and raw frog in Siberia, but the ingestion of water of the Niyodo River of Kochi Prefecture as a causative factor could not be ruled out.

- 64-1012 ADAMANTINOMA OF THE MASTOID PART OF THE TEMPORAL BONE. (E.) Samy, L. L. (Kasr El Ainy Hosp., Cairo U., Egypt). J. Laryng. 78(6):603-611, 1963.

A rare case of adamantinoma of the mastoid in a woman (age 23 when first seen) is presented. A review (10 references) of the subject is also presented. In one published series (C. A. R. Schulenberg) adamantinoma was shown to be more prevalent in the Bantu tribe, a group in which there are gross caries of the teeth.

ERRATA:

- 2(1):#37, 1964. Change journal pagination to read 237-258.
2(1):#152, 1964. Replace last sentence with: For this period most cancer deaths occurred in October (729,362) and November (739,008).
2(2):#219, 1964. Line 1, change first word to Cotinin.
2(4):1964, Author index, page 1, change Druckey, H. to Druckrey, H.

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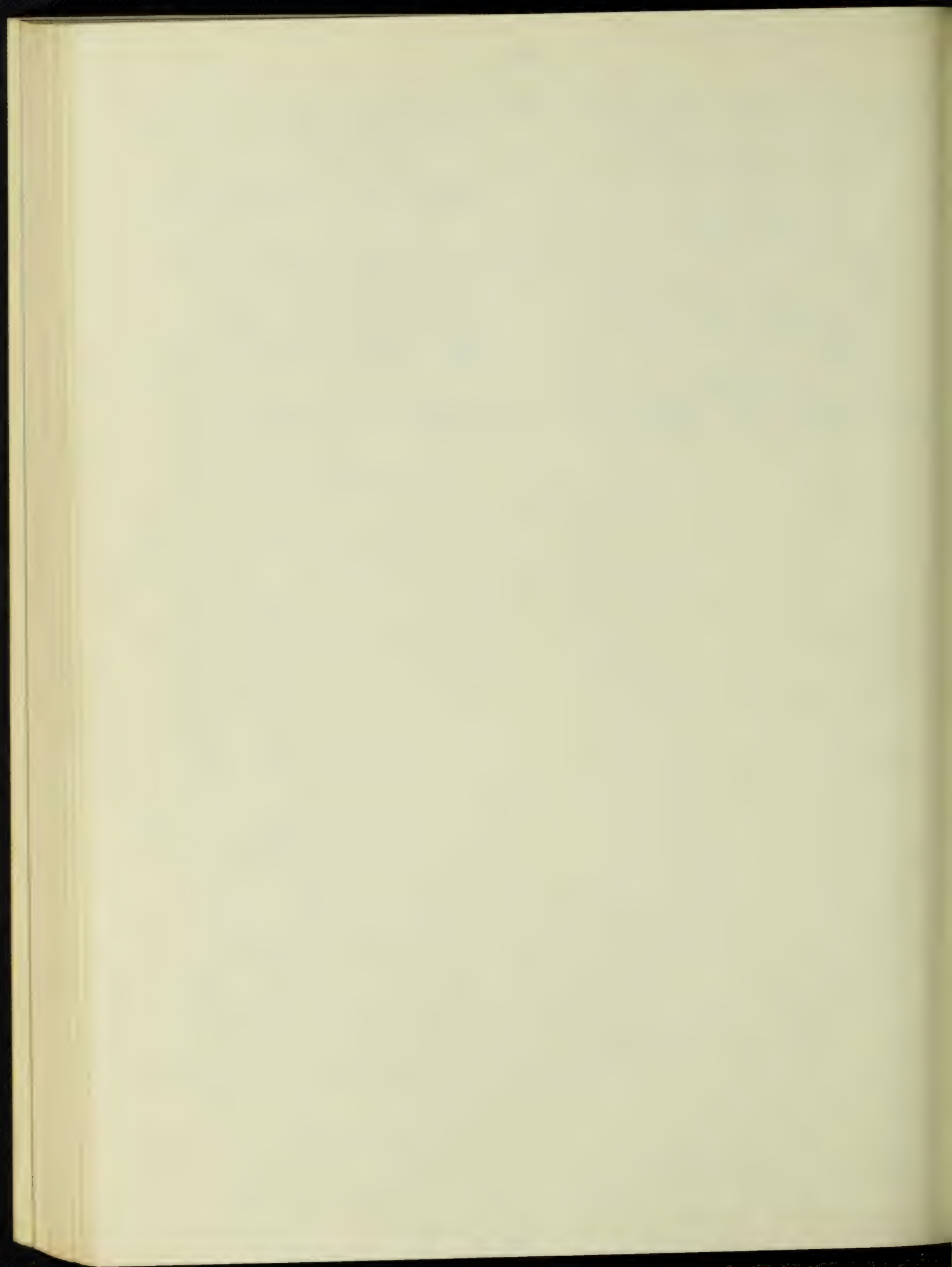
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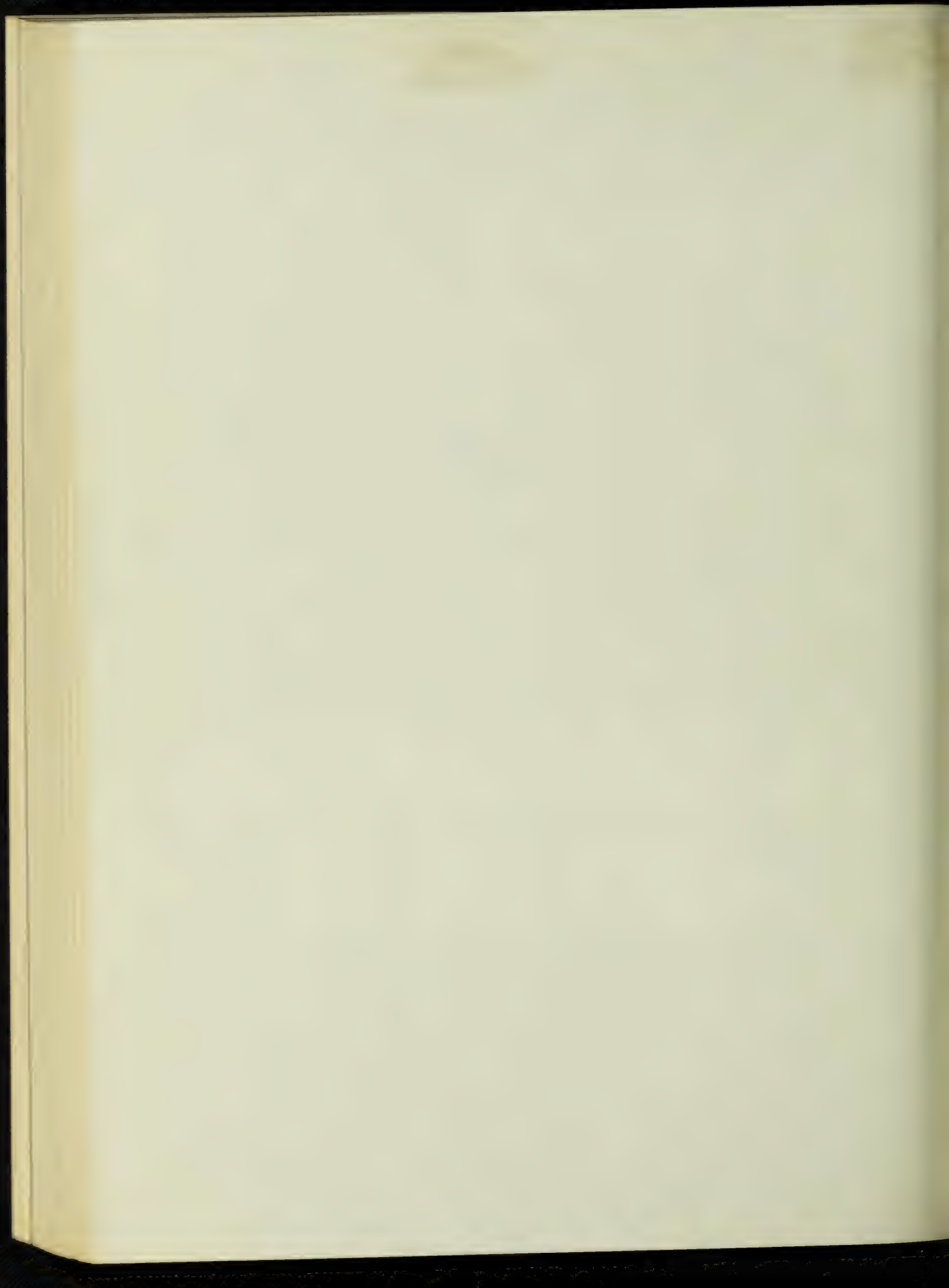
No. 6

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS

ABSTRACTS

Volume 2, Number 6
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

Inquiries may be addressed as follows:

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum, maximal
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubate(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

- 1013 THE GENETICS OF CEREBRAL TUMOURS. (E.)
Koch, G. Acta Neurochir. (Wien)
ppl. 10:24-29, 1964.

A general discussion and review of the influence of genetic influences on the development of brain tumors in which observations on neurofibromatosis and tuberous sclerosis are discussed, the author reports observing the case of a family in which the mother died of a glioma of the parieto-occipital lobe. In the daughter there was a glioblastoma multiforme of the left frontotemporal lobe and the son had a cystic glioblastoma of the right temporal lobe. In another, later, observation 3 sisters died at the ages 50-54 of glioblastoma multiforme. The author discusses these observations in terms of present thought holding that there probably are genetic factors involved which become manifest at the time of change in hormonal environment. (3 references)

- 1014 INDUCTION OF LEUKEMIA BY CHEMICAL AND PHYSICAL NOXAE. (Ger.) Stich, W.
H. Ehrhart. Pp. 660-693 in Handbuch der Hämatologie (Handbook of General Hematology). Vol. 4. Special Hematology. Pt. 2. Meyer, H. C. L. and A. Hittmair (Eds.).
Springer and Schwarzenberg (Publ.) Munich., 693 pp., 1964.

A general review contains sections on benzene, aromatic amines, polycyclic hydrocarbons, steroid hormones, synthetic estrogens, other medications, radiation and exposure to radioactive substances. In discussing radioactive fallout, the authors conclude that the conc. of "hot" by-products (including Sr^{90}) to which Europeans have been exposed thus far is insufficient to constitute a significant health hazard, and that even if one should assume that exposure to very small amounts of radiation exerts the same leukemogenic effect as exposure to high doses (which has been tested, but not proved), the probability of even one European individual's falling ill of leukemia would be increased only from 3.5×10^{-3} to 5.6×10^{-3} . (Approx. 350 references)

- 1015 A LYMPHOMA SYNDROME OF CHILDREN IN TROPICAL AFRICA (BURKITT TUMOUR).
Smyth, H. S. Queen's Med. Review 11:31-38, 1963.

A brief review and discussion on the pathology, prognosis and treatment of Burkitt's tumor. The author notes that the tumor affects both males and females, and is almost unknown before age 5 yr. and extremely rare after age 14 with a peak incidence at 5 yr. This is not a tumor of African children, but rather, a tumor of children in tropical Africa. Of the first 150 cases recorded, 2 were Asian; 1 case was a child of an

Eurasian mother and an European father. Geographically, the tumor is limited to an area stretching across equatorial Africa, from Dakar in the West to Tanganyika and Mombasa in the East, with a small tail running down the east coast on the plains of Mozambique. (5 references)

- 64-1016 ALKYLATING AGENTS. (E.) Brookes, P.
(Chester Beatty Res. Inst., London) and
P. D. Lawley. Brit. Med. Bull. 20(2):91-95, 1964.

In a review and discussion on carcinogenesis and mutagenesis by alkylating agents, it was noted that the ability of alkylating agents to react with a variety of groups within the cell allows them to fit into almost any theory of carcinogenesis. If it be assumed that the carcinogen which remains bound in the cell, rather than being eliminated by metabolism, is responsible for the neoplastic change, then the low level of this binding suggests either that the significant site of reaction is a large molecule, such as DNA, or that considerable selectivity of reaction with smaller molecules occurs. Alkylating agents may be relatively weak carcinogens from a lack of such a selectivity. Bifunctional agents may yield a higher proportion of mutants by deletion of one or more base pairs in DNA. (45 references)

- 64-1017 RADIATION CARCINOGENESIS. (E.)
Lamerton, L. F. (Royal Cancer Hosp.,
Sutton, Surrey, England). Brit. Med. Bull.
20(2):134-138, 1964.

In a discussion and review on the incidence of tumor in irradiated human populations, the author finds that there is, as yet, little evidence of appreciable life-shortening following radiation exposure. In so far as age dependence is concerned, there is a close relationship between radiation-induced and spontaneous incidence of malignant disease. There is evidence with certain types of leukemia that the effect of radiation is largely exhausted after a given time. A higher proportion of prenatal radiodiagnostic examinations was found among the mothers of children affected with childhood leukemia and malignancy than among mothers of control children. Also discussed is the significance of gross chromosome abnormalities and theoretical considerations relevant to radiation carcinogenesis. (26 references)

- 64-1018 THE ETIOLOGY OF BRONCHOGENIC CARCINOMA.
(E.) Ochsner, A. (Ochsner Clin.,
New Orleans). Dis. Chest 45(6):586-590, 1964.

The author reviews and discusses the rise of bronchogenic cancer from the status of a rare disease 25 yr. ago to that of the most common of all visceral carcinomas: according to H. L. Lombard in Massachusetts, the rate of bronchogenic

cancer increased from 3.08/100,000 population in 1930 to 42.16 in 1955, during which time the rate of breast cancer increased from 29 to 36/100,000; in 1930, there were 2,500 deaths from bronchogenic carcinoma in the U. S., as compared to 40,000 in 1962; in 1930, cancer of the lung represented 2.2% of all malignant disease, as compared to 15% in 1960. Studies have shown that neither influenza infection nor smog are of etiologic significance in bronchogenic carcinoma. The increased incidence of bronchogenic cancer, however, definitely parallels the increased use of cigarettes. (21 references)

- 64-1019 ENDOCRINE DYSFUNCTION IN MALIGNANT DISEASE. (E.) Rashad, M. N., (Dept. Anat., Queen's U., Belfast, Ireland). Lancet 1:672-673, 1964.

In a brief discussion of various endocrine disturbances associated with malignant disease, the author advances an explanation of the process of carcinogenesis based on a modification of specific protein synthesis which leads to an accumulation of abnormal protein complexes and excitement of an immune reaction. When a strain of cells lacking the specific antigen arises as an adaptation to continuous attack by a non-lethal antibody, the cells are no longer identifiable, can proliferate regardless of tissue boundaries without being destroyed and so escape into malignancy. Hormone production by malignant cells can be related to alteration of the specific protein synthetic mechanisms which may lead to changes in the enzyme pattern of the tissue, resulting in its ability to produce hormones. (17 references)

- 64-1020 SMOKERS WHO COUGH. (E.) Editorial. Canad. Med. Ass. J. 89(21):1099-1100, 1963.

In a review of clinical studies, some evidence indicates that the greater association of chronic bronchitis with lung cancer is found even when smoking habits are matched. However, there is good clinical evidence that cigarette smoking contributes to chronic obstructive disease of the lung, especially emphysema. (8 references)

- 64-1021 THE ETIOLOGY OF LEUKEMIAS, LYMPHOMAS, AND CANCER. A UNIFYING CONCEPT AND ITS RELATION TO THE AGING PROCESS. (E.) Osgood, E. E. (Dept. Exptl. Med., U. Oregon Sch. Med., Portland). Geriatrics 19(3):208-221, 1964.

A review which attempts to explain the etiology of cancers chiefly through the interaction of 2 types of cells (1) alpha (germ) cells and (2) "n" cells which become functionally mature and may or may not divide; the latter are modified by specific inhibitors, one of which appears early, the other, late in life. (29 references)

- 64-1022 LUNG CANCER IN EUROPE. REPORT ON LUNG CANCER IN SMOKERS. (Fr.) Ertug and Firnberg. Med. Hyg. (Geneve) 22(647):597-599, 1964.

In a report presented to the Consultative Assembly of the European Council, statistics from various European countries on mortality due to cancer of the respiratory tract are compiled and discussed, with emphasis on Austrian studies. In addition to tobacco smoke, dust and industrial waste gases are listed as the main causes of the increasing incidence of lung cancer in Austria and other European countries. It is suggested that methods be established by which air contamination in a given environment can be measured with reasonable accuracy, so that tolerance limits can be determined and remedial measures devised. (5 references)

- 64-1023 STUDIES ON IMMUNOPROPHYLAXIS IN EXPERIMENTALLY INDUCED CANCER. (Fr.) Maisin, J. (Cancer Inst., Catholic U. Louvain, Belgium). Bull. Acad. Roy. Med. Belg. 4(3):197-245, 1964.

The author reviews the work of his own and that of others dealing with the acquisition of new antigens during carcinogenesis, their location and isolation from cell fractions, the resistance that their inj. produces to the inducing agent and the role of neonatal thymus relative to resistance to the skin cancer producing properties of 20-methylcholanthrene in the mouse. (See also CRA 2(3):#472; and *ibid.*, #473, 1964 and earlier papers.) (47 references)

- 64-1024 PROPHYLAXIS OF TOBACCO POISONING. (Fr.) Marti, T. (12 Michel-Chauret St., Geneva, Switzerland) and J. Matasar. Praxis 53(24):828-835, 1964.

The toxic effects of nicotine and tar products contained in tobacco are described in detail on the basis of literature reports; one of the authors, who smoked about 100,000 cigarettes within 4 yr., experienced their ill effects firsthand. American and British statistics on mortality due to diseases of the respiratory system, including bronchial cancer, in smokers and nonsmokers are analyzed, and it is concluded that prophylactic measures are imperative. Various methods of reducing tar and alkaloid content of tobacco are discussed; the characteristics and effectiveness of 12 commercially available cigarette filters are described. (42 references)

- 64-1025 THE PHYSICIAN AND TOBACCO. (Fr.) Jallut, O. (7 Avenue Théâtre, Lausanne, Switzerland). Praxis 53(24):822-827, 1964.

A review of the pertinent experimental and statistical data clearly indicates the carcinogenicity of

...cigarette smoke; nevertheless, smokers (including physicians) are not easily persuaded to give up cigarette smoking. Since no help can be expected from the state or the industry, it is up to the physician to set an example for his pts. by heeding his own advice and giving up the habit, instead of urging them to "do as I say, not as I do." (8 references)

1026 PLANT TUMORS AND THE CANCER PROBLEM. (Ger.) Bergmann, L. (Inst. Plant Biol., U. Göttingen, Germany). Zeitschrift für Naturwissenschaften 51(14):325-332, 1964.

A review of work on the induction of plant tumors following wounding followed by bacterial infection of the wound and the effect of various chemicals on the growth of plant tumors. (32 references)

1027 LUNG CANCER AND ATMOSPHERIC POLLUTION. (Dut. & E.) Editorial. Med. Proc. (Groningen) 10(12):237-241, 1964.

A discussion of statements of Prof. F. C. Pybus (of Newcastle-upon-Tyne) on cancer and atmospheric pollution is presented. The high incidence of lung cancer is blamed on the atmospheric pollution and the dangers of cigarette smoking are minimized. Various statistics are interpreted to show no correlation between smoking and lung cancer, and it is claimed that the late statistician, Sir Ronald Fischer, stated that inhaling cigarette smoke may actually prevent lung cancer. (No references)

1028 INDUCTION BY ASSOCIATION. (E.) Editorial. Brit. Med. J. 1:1395-1396, 1964.

A review calls attention to the fact that the virus in tumors, whether it is present as complete infective particles or as extractable inactive nucleic acid, is produced in only minimal amounts. It now seems probable that if some human neoplasms are caused by viruses there may not be sufficient amounts in tumor cells to be extracted by conventional techniques. In the work of B. Sabin and M. A. Koch (see CRA 1(11):1, 1964) living tumor cells *in vitro* were associated with cells susceptible to the virus; the latter were only required to show a cytopathic effect. Sabin and Koch believe that their

data provide a new approach to the search for viruses in human cancers. (See also CRA 2(5):#936, 1964.) (17 references)

64-1029 CHRONIC SKIN CHANGES DUE TO LIGHT. (Ger.) Ippen, H. (Skin Clin., Acad. Med., Düsseldorf, Germany). Strahlentherapie 123(4):622-631, 1964.

A review and discussion of skin changes due to sunlight in reference to geographic and racial pathogenic factors are presented (e.g., carcinogenic effects of high intensity of sunlight or prolonged exposure to therapeutic UV light, and low amounts of pigment in skin). Animal experiments are detailed and protective measures are discussed. (No references)

64-1030 FOCAL REACTIONS AND CARCINOMA. (Ger.) Kretz, J. Krebsarzt 19(2):92-96, 1964.

A discussion is presented of the influence of focal reactions on the pathogenesis and progression of many cases of lingering illness as well as cancer. Variable response to treatment shows the significance of the body's own defense reactions. The tumor may become a focus, and, mainly in those showing enhanced growth or where secondary inflammatory complications occur, and cause disturbances at a distant site. Such foci, which may disturb the defense mechanism, could be situated elsewhere in the body. (See also CRA 1(5):#801, 1963.) (7 references)

64-1031 AIR POLLUTION, LUNG CANCER, AND CHRONIC LUNG DISEASE. (E.) Eckardt, R. E. (Esso Res. & Engineering Co., Linden, N. J.). Med. Bull. Standard Oil Co. (N. J.) 24(2):101-110, 1964.

See CRA 2(2):#188, 1964. (24 references)

64-1032 SMOKING AND ITS INJURIOUS EFFECTS ON HEALTH. (E.) Randhawa, I. H. Pakistan J. Health 13(3):187-193, 1963.

A review of the deleterious effects of smoking, in which the increase in incidence of lung cancer is attributed to increased cigarette consumption (based on British and American studies) and air pollution. (10 references)

See also abstract nos.: 1044, 1174

PHYSICAL CARCINOGENESIS

64-1033 A CASE OF SQUAMOUS CELL CARCINOMA OF THE FEMALE EXTERNAL GENITALIA ARISING 13 YEARS AFTER RADICAL SURGERY AND RADIOTHERAPY FOR CARCINOMA OF THE EXTERNAL GENITALIA. (Jap.) Maruyama, K. (Dept. Obstet. Gynec., Gumma U., Japan), M. Tsukagoshi, M. Kurihara and K. Hosaka. Sanka To Fujinka (Obstet. Gynec., Tokyo) 30(1): 102-104, 1963.

A 48-year-old Oriental female who underwent radical surgery and treatment by extensive X-irradiation for carcinoma of the external genitalia 13 yr. previously developed squamous cell carcinoma in the scar tissue which resulted from the X-irradiation.

64-1034 EXTRAVASATED THOROTRAST AS A CERVICAL TUMOR AND A CAUSE OF HOARSE VOICE. (Jap.). Sato, T. (Dept. Otorhinolaryng., Fac. Med., U. Osaka, Japan) and S. Sugiyama. Nippon Jibiinkoka Gakkai Kaiho (J. Otorhinolaryng. Soc. Jap.) 66(1):35-37, 1963.

Biopsy of a cervical mass in a 36-year-old female pt. with hoarseness due to paralysis of the recurrent laryngeal nerve revealed a granuloma due to Thorotrast deposition. The history revealed use of Thorotrast in an angiographic study approx. 20 yr. previously.

64-1035 X-RAY INDUCED CANCER 20 YEARS AFTER IRRADIATION OF A CHEST WALL. (Ger.) Reinermann, T. (Inst. Radiol., Knappschafts Hosp., Recklinghausen, Germany). Strahlentherapie 123(4):632-637, 1964.

A brief review (32 references) of the frequency of X-ray-induced cancer of skin is followed by discussion and presentation of a case report of a woman who received surgery for a recurrent fibrosarcoma of the thoracic wall and postsurgical irradiation. An X-ray scar developed and an ulcer formed 15 yr. later which was treated for 5 yr. with salves, etc. At biopsy 20 yr. after irradiation, squamous cell carcinoma was found at the borders of the X-ray-induced ulcer.

64-1036 SURVEY OF CHILDHOOD CANCERS. (E., Abstract) Stewart, A. M. Pp. 436-438 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

Of 628 children born between 1952-56 with leukemia or lymphosarcoma, 120 had histories of prenatal irradiation (of whom 7 died before age 1 yr.); of the remaining 508 not exposed prenatally, 75 died the first year. However, as the age of death increased, so did the proportion of X-rayed cases: 15/120 at age 1; 25/120 at age

2; 34/120 at age 3; 39/120 at age 4. According to these findings, approx. 60% of all the children who were X-rayed in utero owed their death to this event. The mean age at death of the children with irradiation-induced leukemias was greater than the mean age at death of the other cases. The minimum incub. period for irradiation-induced leukemia was 13 mo.

64-1037 TUMORS FROM PLASTIC SUBSTANCES AND NEW CANCER THEORIES. (It.) Sirtori, C. Riv. Geront. Ger. 12(5):191-193, 1964.

See CRA 1(12):#2072, 1964.

64-1038 HISTOPATHOLOGY OF BONE IN DOGS GIVEN RADIOSTRONTIUM. (E., Abstract) Biskis, B. O. (Argonne Nat. Lab., Ill.) and M. P. Finkel. Fed. Proc. 23(2)(Pt. 1):393, 1964.

A histologic study has been completed on 16 dogs given the equivalent of 150 μ C/kg of Sr^{90} (admin. the first wk. after birth, at 6 mo. and after adulthood). First appearance of bone damage was in the metaphysis, then in the diaphysis where very abnormal bone was produced between remnants of persistent endochondral bone. Repair included the resorption of bone and its replacement with fibrous tissue or with additional abnormal bone; and was frequently associated with foci of neoplastic growth. Among 11/16 dogs that died between 1.5 and 2.4 yr. of age, 43 independent osteogenic sarcomas were found. (See also CRA 2(3):#435, 1964.)

64-1039 EXPERIMENTAL TUMORS OF THE OVARY IN RATS. (Rus.) Ird, E. A. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow). Biull. Eksp. Biol. Med. 57(3):89-91, 1964.

Tumor frequency in the ovaries of rats X-irradiated with 100-1200 r was dose dependent; 15-64% rats developed tumors and in 32% they were bilateral. First tumors appeared after 11-15.5 mo. In the rats with homotransplantation of previously irradiated or untreated ovaries into the thigh muscle of ovariectomized rats, tumors appeared in 75% and 41%, resp. First tumors appeared after 9.5 mo. In rats with subtotal ovariectomy, tumor frequency was 22%; first appearance was after 12 mo. Controls showed no tumors. Mixed tumors, theca cell luteoma and granulomatous theca cell luteoma were found in 40% and 39%; luteoma was found in 4 and fibrosarcoma in 4. Precancerous changes were found in 32/397 rats. In the rats with precancerous changes hypophyseal gonadotropic activity was increased, while in animals with tumors it was decreased. Induced tumors were successfully transplanted to ovariectomized females with retention of estrogenic activity following transplantation.

1040 IRRADIATION DOSE IN A PATIENT WITH PULMONARY TUBERCULOSIS AND THE PROBABILITY OF RADIATION-INDUCED LEUKEMIA. (Fr.) Ser, P. (34 Vianden St., Luxembourg). Bull. Sci. Med. Luxemb. 101(2):119-125, 1964.

A pt. with tuberculosis of the lung subjected 5 yr. to an estimated X-ray dose of 110 r yr., the appearance of myeloid leukemia was found to have an 89.9-93% probability of being biologically induced. A review of radiologically induced leukemia is also presented (5 references).

1041 ACTION OF ISOLOGOUS BONE MARROW FROM URETHAN-TREATED C57BL/6 MICE ON RADIATION-INDUCED LEUKEMOGENESIS. (E.) Berenblum, I. (Weizmann Inst. Sci., Rehovoth, Israel), Boiato, L. Fiore-Donati and N. Trainin. Cancer Inst. 32(3):723-729, 1964.

Urethan (U; 20 mg x 1 inj. i.p. or 5 inj. intervals of 5-6 days to a total of 100 mg) admin. to C57BL/6 male and female mice, followed 48 hr. after the last inj. with sacrifice inj. of the animals' bone marrow into irradiated (150 r/wk. x 4) mice, the incidence of leukemia in these irradiated males and females was 2/31 (6%) and 5/18 (28%); U (100 mg), 3/25 (12%) and 2/23 (9%) as compared to 0/31 (0%) and 0/36 (0%), resp., for untreated marrow. The incidence of leukemia was 95/137 in irradiated control mice not given bone marrow inoc. There appeared to be no difference in the proportion of leukemic lesions confined to thymus or disseminated to other organs. The results support earlier findings which concluded that the promoting effect of U in leukemogenesis does not depend on the inactivation of the bone marrow. (See also CRA 2(6):#1042, 1964.)

1042 A FACTOR ('RLP') FROM SHEEP SPLEEN WHICH INHIBITS RADIATION LEUKAEMOGENESIS IN MICE. (E.) Berenblum, I. (Weizmann Inst. Rehovoth, Israel), G. Cividalli, M. E. Hodes and N. Trainin. Nature (London) 202:973-974, 1964.

Groups of 10 C57BL/6 mice, age 5-7 wk., were exposed to X-irradiation (150 r/wk. x 4; total 600 r) and subsequently inj. i.p. with sheep spleen fractions (SSF; 0.25 ml/inj. 4 hr. after exposure, then 2 inj./wk. x 3-13 wk.; total 10-26 inj.). The most marked inhibition (69%) of radiation-induced leukemia was with the crude supernatant, while the centrifugated supernatant and precipitate fractions showed significant inhibition (53% and 45%, resp.). Removal of cells by filtration of the supernatant did not significantly lower its inhibiting activity; however, heating the supernatant or heating it to 60° for 1 hr. destroyed most of the activity. These results provide good evidence for the existence of a cell-free radiation-leukemia-protection

factor (temporarily designated 'RLP') in heterologous sheep spleen.

64-1043 SOMATIC RADIATION DAMAGE. (Ger.) Schlungbaum, W. (Dept. Radiol., Spandau City Hosp., Berlin, Germany). Roentgenpraxis 17(7):147-159, 1964.

A brief historical review of the effects of radiation on humans is presented with mention of the higher incidence of neoplasms among workers exposed to ionizing radiations; also reviewed are some of the late carcinogenic effects of radiations, such as a carcinoma developing in a pt. irradiated for lymph node tuberculosis.

64-1044 THE THOROTRAST PROBLEM. (Ger.) Blümel, G. (1st Dept. Surg., U. Vienna, Austria), R. Lehner and W. Zaunbauer. Wien. Med. Wschr. 114(20):345-348, 1964.

After inj. with Thorotrast (T) about 20 yr. previously, 5 pts. were examined for thorium deposits. In addition to deposits in liver, spleen and lymph nodes, superficial local deposits were found after paravascular inguinal inj., while intravascular inj. had produced deposits in the RES only; none of the cases showed evidence of malignant degeneration. Literature reports on T radiation are reviewed (16 references) and the data on radiation exposure of individual organs after T admin. are recalculated. It is concluded that a correlation between T exposure and tumor development can be assumed only when the following criteria are fulfilled: (1) presence of thorium granules in the immediate vicinity of the tumor; (2) latent period of 10-20 yr.; (3) radiation dosage sufficiently great to produce malignant tumors.

64-1045 LATE EFFECTS AFTER THOROTRAST INJECTION. (Ger.) Schlager, K. (Inst. Radiol., Wilhelmin Hosp., Vienna, Austria). Radiol. Austria. 14(4):285-293, 1963.

Four cases are presented which showed evidence of storage of Thorotrast (T). A male (aged 50) after admin. of T 21 yr. previously, showed a granuloma; a male aged 63 after admin. of T 33 yr. previously developed a prostate carcinoma with no apparent connection to T. A woman, aged 55, 20 yr. after T developed a hypernephroma considered probably connected with T; another aged 62, 17 yr. after admin. of T developed a carcinoma of the bile duct thought almost definitely to be connected with T.

64-1046 TUMORS AS LATE MANIFESTATIONS IN WISTAR-KRAT OFFSPRING AFTER TOTAL BODY IRRADIATION ON DAY 9 OF PREGNANCY. (Ger.) Wegner, G. (Dept. Surg., U. Marburg, Germany) and E. H. Graul. Strahlentherapie 123(4):609-613, 1964.

Besides a 40% incidence of brain and eye malformations, late tumors (sarcomas and carcinomas at 13-24 mo.) occurred in 10/98 of the first generation (F₁) of Wistar rats after irradiation of their mothers on day 9 of pregnancy; 3/98 developed benign tumors at 22-26 mo. Both the F₂ generation of the irradiated rats and the controls had spontaneous tumor rates of 3-4%; no malformations were present in F₂ rats.

- 64-1047 CIGARETTES AND POLONIUM-210. (E.) Radford, E. P., Jr. (Kresge Ctr. Environ. Health, Harvard Sch. Public Health, Boston, Mass.) and V. R. Hunt. Science 144: 366-367, 1964.

Polonium-210 (Po²¹⁰) is probably an initiator of bronchial cancer either by virtue of its anticipated low alpha radiation dose in cigarette smoke or by an associated action of radiation and viruses, or by action with cocarcinogens in the smoke. In a discussion of previously published calculations (as reported in CRA 2(2):#195, 1964) it was concluded that more complete data are required to determine bronchial retention times of Po²¹⁰. Proposals were made for standardization of cigarette testing and for identification of scientists who publish such findings.

- 64-1048 A CASE REPORT OF THOROTRAST-INDUCED CHOLANGIOCARCINOMA OF THE LIVER. (Jap., Abstract) Momose, G. (Dept. Int. Med., Toyohashi City Hosp., Japan), T. Akiyama, S. Furuhashi and T. Suchi. Nippon Naika Gakkai Zasshi (J. Jap. Soc. Intern. Med.) 52(6):718, 1963.

A case is reported of a 53-year-old Oriental with a Thorotrast (T)-induced cholangiocarcinoma who had a cerebral angiography with T performed 30 yr. previously because of a head injury. Deposits of T were seen in the liver, spleen and lymph nodes.

- 64-1049 INDUCTION OF LEUKEMIA IN GERMFREE MICE BY X-RAYS. (E.) Pollard, M. (Lobund Lab., U. Notre Dame, Indiana) and T. Matsuzawa. Am. J. Path. 44(6):17a, 1964.

Seven mo. after the first of 4 doses of X-irradiation (whole-body, 150 r/wk. x 4) 14/26 (53%) of germfree (GF) and 7/21 (33%) conventional C3Hf mice developed leukemia. The lesions in both groups of mice resembled those described by others in conventional animals. This represents the first evidence of a disease producing agent in GF mice, and supports the proposition that X-ray-induced leukemia of mice may be perpetuated in the population by either transovarial or trans-placental passage.

- 64-1050 TUMOR INCIDENCE AFTER TOTAL BODY EXPOSURE TO ROENTGEN RAYS UNDER CONDITIONS OF HUNGER AND THIRST. (Ger.) Reincke, U. (Inst. Radiol., U. Freiburg i. Br., Germany), W. Hunstein and E. Stutz. Naturwissenschaften 51(9):221-222, 1964.

In a series of experiments with Wistar rats of both sexes, Group I was fasted 11 days and was irradiated on day 10 of the fast; Group II received only dry feed for 8 days (the feed was rejected after 2-3 days because of thirst), the rats were irradiated on day 7, then physiologic saline was given as the first fluid on day 9; Group III consisted of irradiated controls, Group IV of non-irradiated controls. Incidence of tumor bearers in the resp. groups was: females, 50/57, 51/58, 58/65, 36/81; males, 26/55, 24/58, 13/48, 12/91. The numbers of malignant and benign tumors in the resp. groups, were: females--15 and 122, 18 and 92, 22 and 88, 11 and 39; males--10 and 16, 17 and 13, 7 and 3, 8 and 3. Thus, in comparison to irradiated controls, the incidence of tumor bearers and the number of tumors were significantly increased by hunger and thirst among males but not in females.

See also abstract nos.: 1017, 1080, 1081, 1109, 1139, 1151

CHEMICAL CARCINOGENESIS

1051 CHANGES IN SOME ENZYMATIC ACTIVITIES AND -SH GROUP CONTENT IN THE EPIDERMIS OF MICE UNDERGOING CARCINOGENESIS BY METHYLCHOLANTHRENE. (Ch.) Li, S.-O. (Dept. Biochem., Inst. Exptl. Med., Chinese Acad. Med. Sci., Peking), T.-C. Chao, H.-Y. Chang and S.-Y. Yü. *Acta Biochim. Biophys. Sinica* 2(3):163-172, 1962.

During the course of epidermal carcinogenesis by dimethylcholanthrene (0.6% in acetone, 1 drop 2-3, 2 drops x 24-30) at the rate of 3 times/wk., the following was observed: tissue protein slightly increased; the activity of glutamic dehydrogenase (GDH), glutamic oxaloacetic acid transaminase and glutaminase (phosphate-activated) decreased to 37%-55% of normal, lactic dehydrogenase (LDH) increased 155%-238%, trypsin and dipeptidase activity increased in epidermal tissue while decreasing slightly in papilloma and tumor tissue; ATPase showed no change. The GDH decrease appeared 24 hr. after single application and before either hyperplasia or any change in LDH occurred. Total SH groups remained constant; however, in hyperplastic epidermis the protein-bound SH groups decreased while the nonprotein-bound groups declined. In papilloma and tumor tissue the nonprotein-bound SH increased while protein-bound SH showed no change. Anthracene had no effect on epidermal glutamic or lactic dehydrogenases while crotonaldehyde decreased their activity.

1052 STUDIES ON THE BIOCHEMICAL MECHANISM OF HEPATOCARCINOGENESIS: EFFECTS OF DIFFERENT AZO-DYES ON THE ENZYME ACTIVITY OF RAT LIVER. (Ch.) Li, S.-O. (Dept. Biochem., Inst. Exptl. Med., Chinese Acad. Med. Sci., Peking), S.-Y. Yü, R.-S. Tang and F. Yen. *Acta Biochim. Biophys. Sinica* 3(3):256-270, 1963.

A comparative enzymatic study of the effects of 2-amino-3-methyl-6-methylcholanthrene (2-AMC) and 3'-MeDAB indicates that they are metabolized differently by the liver. In the 2-AMC-induced liver tumor, the activity of glucose-6-phosphate dehydrogenase, 6-phosphogluconic dehydrogenase and dipeptidase (glycyl-L-alanine as substrate) increased, while the activity of glutamic dehydrogenase, glutaminase (phosphate-activated) and ornithine carbamyl transferase decreased. There was no significant change in dipeptidase activity when DL-alanyl-L-glutamate was used as substrate. The activity of tyrosine aminotransferase and tyrosine transaminase were not very different from the controls. Glutamate reductase activity was similar in the normal liver to that of the tumor liver, but it decreased from the 4th to the 13th wk. of carcinogen feeding. Both the protein and nonprotein-bound SH groups were lower in the hepatoma than in the normal liver. Threonine dehydratase was not influenced by the nutritive factor of the diet but the effect of 3'-MeDAB on it

could not be observed during carcinogenesis.

Changes in enzyme activity in the precancerous stage followed those in liver tumors. 2-MeDAB, a non-carcinogen, had no apparent effect on the above enzymes except that glutamic dehydrogenase increased in activity. It is suggested that the specific effect of 3'-MeDAB on the liver enzymes may be closely related to its carcinogenic properties.

64-1053 HISTOLOGICAL AND HISTOCHEMICAL STUDY OF THE EARLY CHANGES IN THE RAT LIVER DURING p-DAB-INDUCED CARCINOGENESIS. (Ch.) Li, C.-T. (Dept. Histol., Peking Coll. Med., China) and D.-R. Chen. *Acta Anat. Sinica* 5(3-4):288-295, 1962.

Addition of DAB, 0.06 g/100 g of the basic diet, induced hepatomas in all of 16 treated male adult rats after 8-12 mo. The cytoplasm of liver parenchymal cells showed decreased basophilia and the appearance of "inclusion bodies" formed by the accumulation of acidophil granules after 7 days. The epithelium of the interlobular bile duct proliferated as the parenchymal cells degenerated until, after 28 days, they invaded the periphery of the liver lobules. Degenerating parenchymal cells showed decreased RNA, glycogen, protein-bound SH, succinic dehydrogenase and non-specific esterase; fat globules appeared in the cells and there was an increase in alkaline phosphatase (ALP). The RNA, SH content and esterase activity all increased in the proliferating duct cells. These young cells were strongly positive for ALP. Histochemically, the "inclusion bodies" were negative for RNA, while positive for the PAS reaction and for SH groups; ALP was not altered.

64-1054 EFFECTS OF SODIUM BROMIDE AND CAFFEINE ON THE INDUCTION OF PITUITARY ADENOMAS BY ESTROGEN IN CHINESE HAMSTER. (Ch.) Liu, C. (Dept. Physiol., Chinese Acad. Med. Sci., Peking). *Acta Physiol. Sinica* 26(3):205-210, 1963.

By increasing the latent period and decreasing the tumor wt., NaBr and caffeine inhibited the development of pituitary chromophobic adenomas caused by α -estradiol or α -estradiol dipropionate (25 μ g in olive oil s.c. 2x/wk.). Among 55 Chinese hamsters receiving estrogen alone, 36 developed adenomas. The s.c. inj. of NaBr or caffeine reduced the tumor incidence to 14/56 and 6/21, resp. The most effective doses were 25 or 40 mg 2x/wk. of NaBr (5% soln.) or 2.5 mg 2x/wk. of caffeine sodium benzoate (0.25% soln.). Some inhibition by NaBr occurred even when admin. was begun 3 mo. after the beginning of α -estradiol inj. However, the prolonged usage of NaBr produced hypertrophy, hyperplasia and adenomatous growth of the thyroid gland.

- 64-1055 OZONOLYSIS OF POLYCYCLIC AROMATICS. XI. 3-METHYLCHOLANTHRENE. (E.) Moriconi, E. J. (Dept. Chem., Fordham U., New York) and L. B. Taranko. *J. Org. Chem.* 28(10):2526-2529, 1963.

The results of some 40 ozonolyses, etc., runs made on a fairly large quantity of 20-methylcholanthrene (MC) are reported. To ozone, MC reacts significantly as a 7,8,9-trisubstituted 1,2-benzanthracene derivative with predominant ozone attack occurring at the L-region.

- 64-1056 PATHOGENESIS OF SPONTANEOUSLY OCCURRING AND INDUCED MELANOTIC AND AMELANOTIC GRANULOMA IN *DROSOPHILA MELANOGASTER*. (E., Thesis, U. Microfilms, Inc., No. 63-7200). Rottino, A. (New York U., New York). *Dissertation Abstr.* 24(5):1803, 1963.

By extensive studies of "melanotic tumors", common in many strains of *Drosophila*, it was concluded that this is a granuloma. All lesions, regardless of how they were produced (human and mouse extracts, various organic and inorganic substances) had identical appearances. The pathologic process could be traced from hyperplastic nodes with formation of hematocytes and migration of these into the body cavity and aggregation into cell masses that disintegrated, became melanized and encapsulated.

- 64-1057 BENZENE-INDUCED HEMOPATHY. THREE CASES OF CHRONIC BENZENE INTOXICATION, TWO OF THEM FATAL. (ACUTE LEUKEMIA AND ACUTE PANCYTOPENIA.) (It.) Gallinelli, R. (Inst. Path. Spec. Med., U. Modena, Italy) and A. Traldi. *Med. Lavoro* 54(3):169-182, 1963.

Among 3 pts. who developed benzene-induced pancytopenia were 2 sisters (aged 27 and 30 yr.) who had worked for 12 and 16 yr., resp., in a pocket-book factory where the adhesive used contained approx. 51% benzene (the younger pt. had only been in contact with the adhesive for 4 yr.). Both sisters, on becoming pregnant, developed a pancytopenia which responded only slightly to therapy but was greatly improved upon termination of pregnancy (by delivery of a living and well baby in the one case and spontaneous abortion in the other). The younger sister was well 3 1/2 yr. after delivery, but the older sister, who became pregnant again 8 mo. following the abortion, developed acute leukemia in addition to the pancytopenia and died of her disease. The importance of pregnancy as a disposing and aggravating factor in benzene hemopathy is discussed.

- 64-1058 THE BIMODAL AGE DISTRIBUTION OF PATIENTS WITH MAMMARY CARCINOMA. EVIDENCE FOR THE EXISTENCE OF 2 TYPES OF HUMAN BREAST CANCER. (E.) De Waard, F. (University Hosp., Utrecht, The Netherlands), E. A. Baanders-van Halewijn and J. Huizinga. *Cancer* 17(2):141-151, 1964.

In an attempt to explain the fact that the age distribution of mammary carcinoma is bimodal, the assumption was made that if estrogens play a role in breast cancer formation, there are two possibilities to account for disturbed hormonal equilibrium: (1) ovarian estrogen disturbance or (2) adrenocortical estrogen disturbance. When 204 breast cancer pts. were separated into 2 groups on the basis of the presence or absence of certain features associated with adrenal estrogen production such as obesity, hypertension and decreased glucose tolerance, the results appeared to be in agreement with statistical facts concerning the bimodal age distribution of human breast cancer. The statistical-genetic investigation of the frequency of breast cancer among relatives of 288 breast cancer pts. and of a control group (565) has provided evidence which shows a hereditary tendency for the type of breast cancer associated with obesity and hypertension.

- 64-1059 HORMONE-DEPENDENT TUMOURS OF THE KIDNEY. I. THE OESTROGEN-INDUCED RENAL TUMOUR OF THE SYRIAN HAMSTER. HORMONE TREATMENT AND POSSIBLE RELATIONSHIP TO CARCINOMA OF THE KIDNEY IN MAN. (E.) Bloom, H. J. G. (Chester Beatty Res. Inst., Royal Cancer Hosp., London, S.W.3), C. E. Dukes and B. C. V. Mitchley. *Brit. J. Cancer* 17(4):611-645, 1963.

In a review and discussion (137 references) of the development and factors influencing the growth and induction of estrogen-induced renal adenocarcinoma in hamsters, diethylstilbestrol (DES; inj. or s.c. implantation), estrone and estriol were noted as inducing renal tumors, while some carcinogens such as 20-methylcholanthrene when admin. to hamsters treated with DES reduced the incidence and growth of the renal tumors. 3,4-Benzpyrene can induce renal cortical tumors in male hamsters. Testosterone propionate (T), progesterone (P) or deoxycorticosterone acetate (DA) admin. to DES-treated male hamsters inhibited the induction of renal tumors, while with the transplanted DES tumor, P and DA each reduced growth rate but T appeared to accelerate it. Treatment with cortisone (C; 1.25 mg 3x/wk.) or 17 α -hydroxy-6 α -methylprogesterone acetate (Provera; 2.5 mg 3x/wk.) alone or in combination had no effect in male hamsters bearing 7-day-old Imferon (iron-dextran)-induced Sarcoma CB-4460 or a 12-day-old hepatoma. No tumor inhibition was produced by 4 doses of C (5 mg/100 g) in hamsters with Mill Hill polyoma virus-induced sarcoma, while tumor inhibition was produced only by 6 doses of C which caused marked wt. loss and death. No metastases were seen in any of the animals. Therefore, it is of interest that the hormone-dependent tumors in the hamster and possibly in man may arise in the kidney, an organ not recognized as a member of the endocrine system or as a secondary sex organ. (See also the following abstract.)

- 64-1060 HORMONE-DEPENDENT TUMOURS OF THE KIDNEY. II. EFFECT OF ENDOCRINE ABLATION

PROCEDURES ON THE TRANSPLANTED OESTROGEN-INDUCED RENAL TUMOUR OF THE SYRIAN HAMSTER. (E.) Bloom, J. G. (Chester Beatty Res. Inst., Royal Cancer Hosp., London, S.W.3), W. H. Baker, C. E. Dukes and B. C. V. Mitchley. Brit. J. Cancer 17(4): 646-656, 1963.

In male hamsters with 9-day-old estrogen-independent (EI) renal tumor (see the preceding abstract), treatment with bilateral adrenalectomy (adx.) produced marked to moderate tumor inhibition in some animals; accessory adrenal tissue may have been responsible for this response. Orchiectomy (orx.), however, completely inhibited the development of tumor grafts and prevented further growth of well-established transplants in other groups of hamsters. When adx. animals showing slight tumor inhibition were orx., further tumor growth was prevented and regression occurred. When estradiol monobenzoate (0.25 mg/day s.c.) or testosterone propionate (0.25 mg/day s.c.) were admin. to orx. animals with 7-day-old tumor, the inhibitory effect of orx. on the tumor was completely abolished by the hormones.

4-1061 THE STEROID CONJUGATING CAPACITY OF RAT LIVER DURING HEPATO-CARCINOGENESIS. (E.) Abstract Gallegos, A. J. (Dept. Anat., Utah Sch. Med., Salt Lake City) and D. L. Berliner. Fed. Proc. 23(2)(Pt. 1):520, 1964.

At 15-day intervals (up to 200 days), minced livers of control rats and rats fed a riboflavin deficient diet supplemented with 3-DAB were incub. with C^{14} -estradiol (E) + corticosterone- H^3 (C) in PO_4 buffer pH 7.4 at $37^\circ C$ for 2 hr. with and without $Gl-6-PO_4$ and TPNH. During the first 45 days there was an increase in water soluble steroids (3.8% for E, 15.2% for C) concomitant with RE cell stimulation. After 100 days conjugation of E significantly declined (58%), after 150 days that for C declined to 69%; these changes coincided with connective tissue increase and hepatoma formation with lung metastasis. The steroid changes occurred at least 70 days prior to the diagnosis of hepatoma.

4-1062 TEMPERATURE OF CIGARETTE COMBUSTION UNDER DIFFERENT EXPERIMENTAL CONDITIONS. (E.) Scassellati Sforzolini, G. (Inst. Hygiene, Perugia, Italy) and V. Mastrandrea. Boll. Soc. Ital. Biol. Sper. 39(18):1007-1010, 1963.

In a series of experiments conducted with various filters (Marlboro, Nazionali Esportazione) and non-filter (Pall Mall, Chesterfield, Marlboro) with filter removed, Nazionali Esportazione) cigarettes, the combustion temperature (CT) of the latter group remained relatively constant (av. $640-650^\circ C$), while that of filter cigarettes was lower (av. $612-623^\circ C$). No differences were observed in CT measured during the interval between puffs. In studies on 20 smokers (20 puffs/subject) of both sexes and with different

smoking habits, a pressure drop during puffing of 10 mm Hg was found in occasional smokers and of 40 mm Hg in regular smokers (1 pack/day). Av. CT ($^\circ C$) for filter and non-filter Nazionali Esportazione was 608 and 632 for pressure drop = 10 mm Hg, 623 and 650 for pressure drop = 20 mm Hg, 683 and 697 for pressure drop = 40 mm Hg. Cigarette filters were thus found to lower the CT $15-25^\circ C$, according to smoking habits.

64-1063 EFFECTS OF METHANDROSTENOLONE ON MUSCLE CARCINOGENESIS INDUCED IN RATS BY NICKEL SULPHIDE. (E.) Jasmin, G. (Dept. Pathol. Anat., U. Montreal, Canada). Brit. J. Cancer 17(4): 681-686, 1963.

Young female Sprague-Dawley rats were treated with a single inj. of NiS (0.1 ml of a 10% aqueous suspension in right gastrocnemius) alone or + methandrostenolone (MA; 0.5 mg/d x 217 s.c.). The incidence of NiS-induced rhabdomyosarcoma was 100% (10/10) in the MA-treated animals and the tumor appeared first at 137 days as compared to 33% (5/15) and 149 days in the NiS controls. The distribution of metastases in the MA-treated animals was pelvic organ lymphatics 2/10, abdominal wall lymphatics 2/10, aortic lymph glands 10/10, lungs 8/10, and 1 each spleen, heart, and kidney as compared to distribution in controls of 0/15, 0/15, 2/15, 1/15, 0/15, 0/15 and 0/15, resp. When Sprague-Dawley rats with transplanted NiS-induced rhabdomyosarcoma were treated with MA (0.5 mg/day x 45 s.c.), both the take and development of the tumor was reduced by MA as shown by an overall av. time of tumor appearance of 32.8 days (untreated controls, 28.5 days) and an av. tumor wt. of 2.66 g (controls, 4.26 g). No metastases were seen.

64-1064 CONNECTIVE-TISSUE TUMORS OF GUINEA PIGS CAUSED BY ADMINISTRATION OF ESTROGENS. (Rus.) Zhuravleva, T. B. (1st Leningrad "I.P. Pavlov" Med. Inst., USSR). Ark. Pat. 26(6): 65-72, 1964.

In a study made on 98 mature female guinea pigs, some of which were previously castrated, Hexestrol (Synestrol) pellets (25 mg) were implanted at monthly intervals. After admin. for up to 330 days, malignant tumor incidence was dependent on dose; most tumors occurred in the wall of the small intestine, uterus, stomach, omentum or mesentery. The tumorous process involved not only the supportive connective tissue, but also the mesothelium, and tissue elements of the vascular system and smooth musculature. In the process of tumor differentiation areas of osseous and cartilaginous tissue were formed. Most of the tumors formed had the structure of a fibroma, fibrosarcoma or spindle cell sarcoma.

64-1065 POSSIBILITY OF THE TUMOROUS TRANSFORMATION OF INTRASPLENIC OVARIAN TRANSPLANT

AFTER THE INHIBITION OF GONADOTROPIC FUNCTION OF THE HYPOPHYSIS. (Rus.) Bordiushkov, Iu. N. (Rostov Inst. Radiol. Oncol., Rostov-on-Don, USSR). *Biull. Eksper. Biol. Med.* 57(6):78-81, 1964.

Two mo. after castration and intrasplenic ovarian transplantation white infantile random bred rats were treated with testosterone propionate (T) for 2 mo. After 7 mo., in the group treated with a small dose (1 mg 2x/wk.) 3 showed granulosa cell tumors, 2 nidal proliferation of lutein cells and 1 cystic degeneration of follicles. In the group treated with a larger dose (5 mg 2x/wk.) transplants were of the same type and consisted of soft corpora lutea, and were without follicles in the first group follicles showed multiple cystic degeneration and corpora lutea were only occasionally found. In this study T depressed hypophyseal gonadotropic function.

64-1066 EXPERIMENTAL INDUCTION OF THYMOMAS AND OTHER LYMPHOID TISSUE ABNORMALITIES IN RATS. (E., Abstract) Simpson, W. L. (Detroit Inst. Cancer Res., Mich.), B. Bond and G. Leithauser. *Fed. Proc.* 23(2)(Pt. 1):393, 1964.

Sprague-Dawley rats subjected to thymectomy (Group I) or a sham operation (Group II) at age 1-4 days, were fed 20 mg of 9,10-dimethyl-1,2-benzanthracene (DMBA) in oil when they reached 160 g (age 7-11 wk.). Group I was sacrificed 120 days, and Group II 180 days after DMBA admin. At autopsy, the thymuses of Group II varied from an occasional normal to those in which entire lobes were replaced by epithelial tissue. In Group I, marked changes were seen in the mediastinal lymph nodes: acute depletion of lymph elements, increased levels of circulating lymphoid cells, acute hemolytic changes and replacement of normal lymphoid tissues by plasma cells.

64-1067 THE POTENTIATION OF LYMPHOSARCOMAS IN THE MOUSE BY MANGANOUS CHLORIDE. (E., Abstract) DiPaolo, J. A. (NIH, Bethesda). *Fed. Proc.* 23(2)(Pt. 1):393, 1964.

Female DBA/1 mice (6-8 wk. old) were inj. s.c. or i.p. with manganous chloride (0.1 ml of a 1% aqueous soln., 2x/wk. for 6 mo.); controls were inj. with water. Animals were sacrificed at the age of 18 mo. or when moribund. Lymphosarcomas were observed in 24/36 (67%) of s.c. treated and 16/39 (41%) of the i.p. treated mice, but in only 16/66 (24%) controls. Tumors appeared earlier in treated mice but did not appear at the inj. site, although some scars were observed there. Increased incidence of lymphosarcoma with $MnCl_2$ suggests a parallelism between mutagenesis and carcinogenesis in the initiation of some tumors.

64-1068 PATTERNS OF GROWTH PRODUCED IN THE GASTRIC WALL BY IMPLANTING 7,12-DI-METHYLBENZ(α)ANTHRACENE (DMBA) WITH AND WITHOUT GELFOAM. (E., Abstract) Grant, R. (Dept. Path., U. Illinois Coll. Med., Chicago) and R. Wong. *Fed. Proc.* 23(2)(Pt. 1):337, 1964.

Rats were implanted with DMBA alone (Group I), DMBA + Gelfoam (Group II) and Gelfoam alone (Group III) and then sacrificed after 148-320 days. The lesions found were of 3 general types: abnormal repair with mucosal glandular metaplasia in 10/12 rats of Group I (153-320 days) and in 4/10 rats of Group II (148-287 days); a sarcomatous pattern in 2/12 rats of Group I (225-256 days) and in 5/10 rats of Group II (242-287 days), as well as 1 liver metastasis and 1 local liver invasion. A mucin-producing adenocarcinoma was seen in 1 rat of Group II (280 days). Neither atypical nor malignant changes were seen in Group III after 211-302 days. The carcinogenic action of DMBA on the rat stomach was found to be greater than that of 20-methylcholanthrene.

64-1069 STUDIES ON THE ROLE OF VIRUS IN LEUKEMOGENESIS BY 20-METHYLCHOLANTHRENE IN RF MOUSE. (E.) Irino, S., (Dept. Int. Med., Okayama U. Sch. Med., Japan), Z. Ota, T. Sezaki, M. Suzuki and K. Hiraki. *Arch. Histol. Jap.* 24(3):285-292, 1964.

A compilation of work previously abstracted in *CRA* 1(8):#1467, 1963; *ibid.*, 1(9-10):#1702; *ibid.*, #1758; and *ibid.*, 1(12):#2153, 1964.

64-1070 PHENYLBUTAZONE AND LEUKAEMIA. (E.) Sen, S. and K. K. H. Siddique. *Bull. Inst. Post Grad. Med. Ed.* 6(1):23-24, 1964.

The authors reported 2 men who received phenylbutazone (PB) over various periods of time prior to diagnosis of leukemia and indicated that PB may have had some leukemogenic effect in 1 pt. This was a 30-year-old Hindu man with chronic myeloid leukemia who was previously treated with radiation, followed 2 yr. later by large doses of PB (about 23,300 mg). The other pt. with sub-leukemic myeloblastic leukemia received only about 9 g of PB for 4 mo. before diagnosis; furthermore, the interval between drug admin. and leukemia was short.

64-1071 FURTHER EXPERIMENTS ON THE EFFECT OF HORMONES AND CARCINOGENS ON THE PROSTATE GLAND IN ORGAN CULTURE. ACTION OF 20-METHYLCHOLANTHRENE ON ORGAN CULTURES OF THE VENTRAL PROSTATE GLAND OF RATS, AND THE INFLUENCE OF HYDROCORTISONE ON THIS EFFECT. (E., Abstract) Lasnitzki, I. P. 396 in *British Empire Cancer Campaign 1963*. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

After exposure of organ cultures of the ventral prostate gland of rats in natural medium to 20-methylcholanthrene (MC), there was provoked extensive epithelial hyperplasia in most cultures and the alveoli became filled with undifferentiated cells lined by secretory elements which were functional until the lumen was occluded. After 14-17 days' growth, the first stage of squamous metaplasia appeared with the formation of prickly cells. Return to normal medium was followed by a reduction of hyperplasia (in contrast to mouse prostate cultures in which hyperplasia progresses further). When MC was used simultaneously with hydrocortisone, the changes produced by the carcinogen were completely inhibited. MC had little effect in a semi-defined medium.

64-1072 STUDIES ON THE CARCINOGENICITY OF TRICYCLOQUINAZOLINE. (E.) Baldwin, R. W. (Dept. Cancer Res., U. Nottingham, England), H. G. Dean, M. Moore, H. C. Palmer, M. W. Partridge, J. A. Shouler, S. A. Storch and H. J. Vipond. Pp. 420-426 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

A fluoro-substitution on the 2-position of tricycloquinazoline (TCQ) caused a lower incidence (23%) of skin carcinomas than did TCQ (75%) after repeated skin applications on mice. As an initiator, 2-fluoro-TCQ caused skin papillomas in 48% of mice following 4 applications (total 1.2 mg/mouse) and subsequent twice weekly treatment with croton oil for 20 wk. Substitutions such as 2-methylation, hydroxylation or methoxylation produced a complete loss of carcinogenicity; whereas substitutions at the 3-position only partially depressed activity. In addition, TCQ-IN and seco-TCQ are both virtually inactive. Yet, when the inactive 2-methyl-TCQ was applied as a mixture with TCQ (total conc. of 1.2 mg), the tumor initiating capacity of TCQ was enhanced. Similar enhancement was produced by 2-fluoro-TCQ and 3-fluoro-TCQ. After i.p. admin. of TCQ, approx. 50% is metabolized in 48 hr., the metabolites being excreted mainly in the feces. In contrast, no appreciable loss is detected following skin applications, indicating that the rate of absorption is probably a limiting factor in TCQ carcinogenicity. (See also CRA 1(3):#415; and ibid., (8):#1532, 1963.)

64-1073 EFFECT OF CARCINOGENIC AMINOAZO-DYES ON THE METABOLIC ACTIVITY OF RAT LIVER MICROSOMES. (E., Abstract) Barker, C. R. (Dept. Cancer Res., U. Nottingham, England) and R. W. Baldwin. Pp. 426-428 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

The oral admin. (dosage not given) of 4-dimethylaminoazobenzene (DAB) to rats for 30 days depressed the enzymatic activity to 5%-50% of normal

levels of 3,4-benzpyrene and 2-acetylaminofluorene hydroxylase, diphenhydramine and aminopyrine N-demethylase and chlorpromazine sulfoxidase in liver mitochondrial supernatant preparations. Likewise, liver microsomal glucose-6-phosphatase and NADH₂-cytochrome c-oxidoreductase (drug metabolizing enzymes) were depressed to 25% and 44%, resp., but 5'-nucleotidase activity was stimulated. The activity of combined liver cell sap-microsome fraction is increased to 40% above normal liver fractions after this 30-day feeding, with greater stimulation in the ribosome fraction. These characteristics do not define the precancerous state since several of these effects are observed with a non-carcinogenic aminoazo dye.

64-1074 CHARACTERISTICS OF A TRANSPLANTABLE THYROID CARCINOMA INDUCED BY THYROTROPIN. (E., Abstract) Sinha, D. K. (Dept. Path., Columbia U., New York). Fed. Proc. 23(2) (Pt. 1):288, 1964.

The cells of highly TSH dependent thyroid tumor (TT) induced in mice by thyrotropin in 1957 and since carried by serial passage, now take up ¹³¹I as rapidly as normal thyroid cells but lose it faster. In contrast to normal thyroid, ¹³¹I distribution in the TT is patchy. Originally predominantly adenomatous and rich in colloid with many papillary areas, colloid production has decreased, papillary areas vanished and now the TT is composed predominantly of oxyphilic "Hurthle" cells. The TT now grows even in euthyroid mice.

64-1075 ABSORPTION AND EXCRETION OF BENZPYRENE WHEN FED TO MICE. (E.) Neal, J. (Dept. Prevent. Med., U. Texas Med. Branch, Galveston) and R. H. Rigdon. Texas Rep. Biol. Med. 22(1):156-164, 1964.

Benzpyrene (BP) was demonstrable spectrophotometrically in the kidney and liver of mice (brown CBA, Mus musculus and Peromyscus maniculatus gambeli) 90 min. after they were fed BP crystals (20 mg/gm of diet). The skin and viscera showed a blue fluorescence after 30-60 min., and the urine after 90 min. appeared blue with UV lighting. There was a progressive decrease of this blue fluorescence when the BP diet was discontinued: there was virtually no fluorescence after 48 hr. in the kidney and urine, after 72 hr. in the viscera and after approx. 10 days in the skin. When smaller amounts of BP were fed there was an increase in the interval necessary for the tissues to show this fluorescence.

64-1076 HORMONES IN LIVER CARCINOGENESIS. (E., Abstract) Yamamoto, R. S. (NCI, Bethesda), S. R. Pai and J. H. Weisburger. Fed. Proc. 23(2) (Pt. 1):105, 1964.

The effect of an anabolic hormone, norethandrolone (NA; 0.007% in a semisynthetic diet) on liver

carcinogenesis induced by N-hydroxy-2-acetylaminofluorene (HAF; 0.008% in the diet), was studied in groups of weanling ACI rats; one group received only HAF. The period of feeding was 14 mo. Weanling F344 rats were fed HAF for 4 wk. prior to transfer to the same groups. NA alone after 10 wk. of HAF slightly increased hepatoma incidence in males but not in females. All groups given NA showed depressed wt. of endocrine organs. Supplementation with dietary thyroid also favored hepatoma formation. (See also CRA 1(11):#1900; and *ibid.*, 2(3):#474, 1964.)

- 64-1077 MECHANISM OF OVALBUMIN (OA) DENATURATION BY NITROSAMINES AND OTHER CARCINOGENS. (E., Abstract) Argus, M. F. (Tulane U. Sch. Med., New Orleans, La.) and J. C. Arcos. *Fed. Proc.* 23(2)(Pt. 1):523, 1964.

Specific rotation of OA at various conc. of dimethylnitrosamine (DMN) gave a sigmoid plot, but, in comparison with compounds examined in an earlier study, there was extensive reversal of optical rotation change beyond 4M DMN. 1,1-Dimethylhydrazine (non-carcinogenic) did not aggregate or unfold OA between pH 4-9. A number of compounds investigated (including I₂, KIO₃ and cysteine + N-ethylmaleimide) enhanced OA aggregation. The data suggest that carcinogen-induced aggregation of OA involves hydrogen bond reinforced sulfhydryl-disulfide interchange utilizing 1-SH masked in native OA.

- 64-1078 "SOLUBILIZATION" OF CARCINOGENS WITH NUCLEIC ACID SOLUTIONS. THE INTERACTION OF p-DIMETHYLAMINOAZOBENZENE WITH RIBONUCLEIC ACIDS. (E.) Marmasse, C. (Lab. Inst. Muscle Res., Marine Biol. Lab., Woods Hole, Mass.). *Nature (London)* 202:1010, 1964.

When an RNA with few nucleotides is reacted with dimethylaminoazobenzene, a red soln. is obtained after filtration on Whatman No. 1 paper, but the sediment on the membrane of the ultrafilter is yellow. A study which relates the sizes of the particles to the electronic configuration of the dye leads one to suppose the existence of a correlation between the size of the particles and the electronic configuration of the dye: most, if not all, of the large particles being yellow (azoid form) and most, if not all, of the small ones red (quinoid form). This finding suggests the existence of a critical distance of approach between the reacting constituents.

- 64-1079 CHEMICAL LINKAGE OF THE CARCINOGEN 3,4-BENZOPYRENE-H³ (BP) TO DNA, POLY A, AND POLY U INDUCED BY PHOTORADIATION AT WAVELENGTHS ABOVE 300 MILLIMICRONS. (E., Abstract) Ts'o, P. O. P. (Johns Hopkins U., Baltimore, Md.), P. Lu, M. P. Schweizer and A. E. Smith. *Fed. Proc.* 23(2)(Pt. 1):217, 1964.

The apparent physical binding constant of BP to

denatured thymus DNA was found to be 10³-10⁴ higher than that of thymine and adenine while that of RNA, Poly A and Poly U was 30-100 fold less. After exposure to photoradiation of wavelengths above 300 mμ in N₂ and at 25°C, over 50% of the BP-H³ remained with the DNA after precipitation and extraction--this product was termed DNA-BP. No degradation of the DNA was observed by analytical ultracentrifugation. After analysis of DNA-BP by various methods (sucrose gradient ultracentrifugation, electrophoresis, hydrolysis with DNase and diesterase) all the results indicated that the BP-H³ had been linked chemically onto the nucleotides with the BP:nucleotide ratio of 1:800-2,000. Similar conclusions were reached from preliminary experiments on radiation of Poly A, Poly U and thymidylic acid with BP-H³.

- 64-1080 THE CARCINOGENIC AND CO-CARCINOGENIC EFFECTS OF PARAFFIN WAX PELLETS AND GLASS BEADS IN THE MOUSE BLADDER. (E.) Ball, J. K. (Dept. Biochem., Dalhousie U., Halifax, Nova Scotia, Canada), W. E. H. Field, F. J. C. Roe and M. Walters. *Brit. J. Urol.* 36(2):225-237, 1964.

When paraffin wax pellets (14-16 mg) or spherical glass beads (30-50 mg, smooth or rough) were implanted into the bladder of albino mice (8-10 wk. of age) and which 1 or more wk. later received 2 doses of urethan 7 days apart (16 mg/dose, intragastric), the incidence of lesions after 37 wk. was greater than in mice without the implants. Of the mice with paraffin implants, 8/54 had neoplastic bladder tumors (carcinoma) when urethan was subsequently admin., 10/62 had neoplastic lesions when only water was admin., and 1/67 had a neoplastic lesion with urethan + cystotomy, but with no transplants. The incidence of neoplastic bladder tumors was greater (9/63) in urethan-treated mice bearing rough beads than in those bearing smooth ones (2/66). When water alone was admin. with rough beads there were 2/67 neoplastic tumors. In both series, the urethan-treated mice showed a high incidence (90.9-100%) of leukemia and lung tumors. In conclusion, regardless of the type of bladder implant, there was no clear added effect of urethan on the changes produced. Proliferative and other changes are also discussed.

- 64-1081 AN ILLUSTRATED CLASSIFICATION OF THE PROLIFERATIVE AND NEOPLASTIC CHANGES IN MOUSE BLADDER EPITHELIUM IN RESPONSE TO PROLONGED IRRITATION. (E.) Roe, F. J. C. (Chester Beatty Res. Inst., Royal Cancer Hosp., London, S.W.3). *Brit. J. Urol.* 36(2):238-253, 1964.

A classification with illustrations presents the gradation of lesions from simple hyperplasia and metaplasia, through benignity to malignancy in mouse bladder epithelium responding to prolonged irritation. Bladder implants of paraffin wax pellets or glass beads (rough or smooth) were left for as long as 40 wk.; additionally, some animals received urethan by intubation (see also CRA

(6):#1080, 1964). Neither squamous carcinoma or distant metastases were observed.

4-1082 IMMUNOLOGICAL STUDIES OF RAT LIVER CELL ANTIGENS DURING AMINOAZO-DYE CARCINOGENESIS. (E., Abstract) Baldwin, R. W. (Cancer Res. Dept., U. Nottingham, England). Pp. 430-431 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

This article presents work previously abstracted in CRA 1(4):#631; and ibid., (7):#1277, 1963), with the addition of a few new factors. It was confirmed that 7 normal liver cell sap antigens and at least 6 microsomal antigens are deleted in DMAB (4-dimethylaminoazobenzene)-induced rat liver tumors. There were also detected a number of abnormal antigens (immunoelectrophoretic studies have demonstrated 3 major and 4 minor components) which do not cross-react with normal liver cell sap. Further subfractionation of the oxxycholate-solubilized tissue fractions has so permitted detection of an abnormal tumor microsomal antigen.

4-1083 CARCINOGENICITY OF N-HYDROXY-4-ACETYL-AMINOSTILBENE. (E., Abstract) Smith, R. D. (Cancer Res. Dept., U. Nottingham, England) and R. W. Baldwin. Pp. 428-430 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

The carcinogenic activity of N-hydroxy-4-acetylaminostilbene (HAAS) was evaluated after admin. several routes: p.o. (see CRA 1(9-10):#1686, 1964); p.o. (12 mg) + topical croton oil; i.p. (12 mg) and 60 mg/kg) and s.c. (37.5 mg/kg). Results of the latter 2 studies were complicated by the acute toxicity of the compound. After s.c. in 6 rats (55%) developed ear duct tumors and developed mammary tumors. When tested as initiators at a p.o. dose of 12 mg, followed by 20 local treatment with 5% croton oil, both HAAS and 4-acetylaminostilbene were inactive with reference to skin papillomas. However, when both compounds were fed for 26 wk. in the diet at 0.17% simultaneous skin painting with croton oil, the incidence of skin tumors was 45% and 35%, resp., compared to 12% in controls. After an i.p. dose of 10 mg/kg of HAAS survival was good and 8 rats (40%) developed ear duct carcinomas, 1 an adenocarcinoma of the intestine and 1 a mammary tumor. These studies indicate HAAS is not a potent mammary carcinogen. The major metabolite of HAAS, N-hydroxy-4-acetylaminostilbene, when admin. p.o. at a dosage of 112 mg, proved to be much less active than HAAS and no tumors have as yet developed (54 wk.).

4-1084 THE ROLE OF THE THYROID GLAND IN HEPATIC CARCINOGENESIS. (E., Abstract) Reuber, M. D. (NIH, Bethesda). Fed. Proc. 23(2) (Pt. 1):336, 1964.

Groups of intact and operated male Wistar rats were fed 0.025% N-2-fluorenyldiacetamide in a semisynthetic diet for 2-wk. periods, alternated with 1 wk. on the basal diet, until 16 wk. of the carcinogenic diet was admin. Hepatocellular carcinoma and cirrhosis were seen in 6/11 intact rats after 36 wk. Such lesions were not seen in orchiectomized (ORX) or thyroidectomized (THYRX) rats. Thyroid powder (0.05%) did not restore carcinogenesis in the THYRX or THYRX-ORX rats. A dose of 0.1% of thyroid powder restored carcinogenesis and cirrhosis in THYRX or ORX rats to that of intact rats (10/11); however, this dose was ineffective in THYRX-ORX rats. No tumors developed in THYRX rats given growth hormone, gonadotropin, adrenocorticotropin, cortisone, progesterone or norethandrolone or in THYRX-ORX rats given testosterone, androsterone or norethandrolone. In the rat it appears that both thyroid and testicular hormones are necessary for development of hepatomas and cirrhosis.

64-1085 CARCINOGENICITY OF ALDRIN AND DIELDRIN ON MOUSE AND RAT LIVER. (E., Abstract) Song, J. (Dept. Path., U. Arkansas Med. Ctr., Little Rock) and W. E. Harville. Fed. Proc. 23(2) (Pt. 1):336, 1964.

Groups of C3HeB/FeJ and CBA/J mice (55 total) received 15 ppm of Aldrin (A) or Dieldrin (D). After 330 and 375 days of feeding, neoplasia developed in 4 C3HeB/FeJ and 3 CBA/J mice. No tumors developed in groups of 15 Holtzman rats fed 0.025% of either A or D or in a group of 15 fed D initially at 15 ppm increased every 2 wk. by 10 ppm until a level of 285 ppm was reached. Liver cell necrosis was produced by A and D within 60 days in both rats and mice; nuclear hypertrophy and abnormal mitoses occurred within 90 days.

64-1086 ON THE BINDING OF THE CARCINOGEN 2-ACETYLAMINOFLUORENE TO RAT LIVER RNA AND DNA. (E., Abstract) Williard, R. F. (Dept. Biochem., U. Tennessee Med. Units, Memphis) and C. C. Irving. Fed. Proc. 23(2) (Pt. 1):167, 1964.

The bound radioactivity to liver nucleic acids 24 hr. after inj. into rats of 2-acetylaminofluorene-9- C^{14} (AAF) was equivalent to 33-40 and 17-28 μ moles of AAF per g of RNA and DNA, resp. After inj. of N-hydroxy-AAF-9- C^{14} , comparable values were 59-82 and 28-33 μ moles, resp. After inj. of 1-hydroxy-AAF-1- C^{14} , bound radioactivity was equivalent to only 0.4-1.4 μ moles/g of nucleic acid.

64-1087 DEHYDROXYLATION AND DEACETYLATION OF N-HYDROXY-N-2-FLUORENYLACETAMIDE BY RAT LIVER AND BRAIN HOMOGENATES. (E., Abstract) Grantham, P. H. (NCI, Bethesda), E. K. Weisburger

and J. H. Weisburger. Fed. Proc. 23(2) (Pt. 1):325, 1964.

Incubation of rat liver and brain homogenates, or the soluble fraction from liver with N-hydroxy-2-acetylaminofluorene- C^{14} for up to 8 hr. gave progressively decreasing levels of this compound. Dehydroxylation and deacetylation (measured by assessment of 2-acetylaminofluorene) were most active in liver homogenate; brain and soluble liver fractions were somewhat less effective. Protein labeling increased with time; those from the liver of males were labeled more intensely than those from female livers. 2-Aminohydroxyfluorene reacted with a variety of proteins.

64-1088 MULTIPLE CARCINOMATA FOLLOWING INGESTION OF MEDICINAL ARSENIC. (E.) Minkowitz, S. (Downstate Med. Ctr., State U. New York, Brooklyn). Ann. Intern. Med. 61(2):296-299, 1964.

The case history is presented of a 21-year-old male with multiple epidermoid carcinomas who had been treated between the ages of 7-10 with Fowler's soln. during a period when he had had Sydenham's chorea.

64-1089 SARCOMAS AT THE SUBCUTANEOUS SITE OF INJECTION OF TRYPAN BLUE IN THE RAT. HISTOLOGIC AND CYTOLOGIC STUDIES. (Fr.) Driessens, J. (Inst. Cancer Res., Lille, France), A. Clay, J. Vanlerenberghe, A. Dupont, L. Adenis and A. Demaille. Bull. Assn. Franc. Cancer 50(2):195-202, 1963.

A more extensive microscopic and macroscopic description (with illustrations) of the sarcomas induced by trypan blue described in CRA 1(2):#234, and ibid., (6):#1067, 1963.

64-1090 INDUCTION OF MAMMARY GLAND TUMORS IN STRAIN C57BL/He MICE BY ISOGRAFTS OF HYPOPHYSES. (E.) Heston, W. E. (NCI, Bethesda). J. Nat. Cancer Inst. 32(4):947-955, 1964.

In female (6-week-old) C57BL/He mice, each bearing 5 hypophyseal isografts under the kidney capsule, mammary tumors occurred in 5/21 at an av. age of 20.2 mo. A Type A and a Type B adenocarcinoma and 1/3 adenoacanthomas were successfully transplanted into normal C57BL females. No mammary tumors were seen in females bearing isografts of only 1 hypophysis or in orchiectomized C57BL/He males implanted with 10% diethylstilbestrol-cholesterol pellets (6-8 mg s.c.), followed 2 wk. later with isografts of either 1 or 5 hypophyses. Nearly all the grafted hypophyses became neoplastic, and could be classified as chromophobe adenomas. Other neoplasms noted were reticulum cell neoplasms of Type A or B, lymphocytic leukemia, hemangioendothelioma of the liver and hepatoma.

64-1091 HEPATOMA AND AFLATOXICOSIS IN TROUT. (E., Abstract) Ashley, L. M. (Western Fish Nutrition Lab., Cook, Wash.), J. E. Halver and G. N. Wogan. Fed. Proc. 23(2) (Pt. 1):105, 1964.

Salmo gairdnerii fed wheat aflatoxins for 6-9 mo. in water at 15°C developed hepatoma or aflatoxicosis. Crude aflatoxin at 0.08 ppm of the diet led to 60% of the livers exhibiting classical multinodular hepatoma which histologically resembled chemical carcinogen-induced hepatoma. Forced feeding of purified B₁ and G₁ compounds (0.03-0.3 mg/kg/day) for 5 days led to death with acute aflatoxicosis at 10-15 days; tentative LD₅₀ total dose was 1.5 mg/kg. While the feeding of fish with heat polymerized non-urea adduct forming fat (1%) led to extensive physiological and histological changes in the body, no hepatoma was seen after 4 mo.

64-1092 INDUCTION OF RAT HEPATOMAS BY AFLATOXIN-CONTAMINATED DOMESTIC PEANUT MEALS. (E., Abstract) Newberne, P. M. (Dept. Nutrit. Food Sci., Massachusetts Inst. Tech., Cambridge), G. N. Wogan and W. W. Carlton. Fed. Proc. 23(2) (Pt. 1):336, 1964.

When 4 lots of expeller or solvent-extracted peanut meals were analyzed for aflatoxins, the following amounts (ppm) were found: Sample A (expeller), 0.3-0.5; Sample B (expeller), 3.0-3.5; Sample C (solvent), 0.005; Sample D (solvent), 1.0. When male rats were fed these meals as 75% of dietary protein for 9-12 mo., incidence of hepatoma was, resp.: 1/7, 5/5, 0/10 and 4/9. Thirty-day feeding experiments in ducklings indicated a similar association of aflatoxin contamination with toxic response.

64-1093 NEW EXPERIMENTAL EVIDENCE OF TUMORIGENIC HORMONAL IMBALANCES. (E.) Lipschutz, (Inst. Exptl. Med., Natl. Health Serv., Santiago, Chile), V. I. Panasevich and A. Alvarez. Nature (London) 202:503-504, 1964.

In mice with ovarian grafts in the spleen, kidney or liver, it was shown that tumors originating in the latter are microtumors while those in the spleen are macrotumors. When 1 ovary was grafted into the spleen and the other ovary into the kidney (or liver) of the same animal, no more than microtumors occurred in the intrasplenic and intrarenal (or intrahepatic) grafts. In another series of experiments, a whole or half an ovary was placed in the apical and caudal splenic poles of BALB mice and 12 mo. later macrotumors occurred in most of the animals. The macrotumors consisted of a luteoma with nodules of granulosa tumor cells or a granulosa cell tumor with luteomatous nodules. The results indicate that the differential tumorigenesis in ovarian grafts at different sites is due to tumorigenic bodily conditions outside the graft site.

4-1094 POSSIBLE CARCINOGENIC PROPERTIES OF FOOD PRODUCTS ADMIXTURES AND PRINCIPLES OF THEIR DETERMINATION. (Rus.) Neiman, I. M. (Inst. Nutrition, Acad. Med. Sci. USSR, Moscow). *Stn. Akad. Med. Nauk SSSR* 19(5):57-63, 1964.

A discussion is presented of the possible carcinogenic effect of various synthetic chemicals used as pesticides for the protection of cereals, fruits and vegetables, or to enhance the fattening of cattle or to improve the appearance, color or taste of products or to improve their keeping qualities; also discussed are substances which may get into food products during packaging and processing. Possible carcinogenic properties of fats subjected to long and repeated heating during food preparation is emphasized. "Permissible" doses of carcinogenic substances do not exist. The hazards involved in long-term introduction into the organism of these additives due to cumulative action are pointed out. Research methods used in the study of carcinogenic chemicals used in the food products are indicated.

1095 METABOLIC ANTAGONISM BETWEEN AN AZO DYE AND RIBOFLAVIN: EFFECT OF 3'-METHYL-4-MONOMETHYLAMINOAZOBENZENE ON MUTANTS OF *NEUROSPORA CRASSA*. (E.) Salzberg, D. A. (Inst. Microbiol., U. San Francisco, Cal.). *Cancer Res.* 24(4):619-625, 1964.

The azo dye 3'-methyl-4-monomethylaminoazobenzene (3'-ME-MAB) at a given conc. shows variable inhibition on the growth of riboflavin-independent mutants of the ascomycete fungus, *Neurospora crassa*. This nonspecific inhibition was least at suboptimal conc. of the required nutrient and was not affected by the addition of riboflavin to the medium. With strains requiring riboflavin a reversal is brought about by this addition. Data are also presented showing the inhibitory effect of the required nutrient to restore growth of choline, lysine, methionine or isoleucine-arginine mutants, when these were inhibited by 3'-ME-MAB.

1096 INDUCTION OF SARCOMATA IN RABBITS BY INTRAMUSCULAR INJECTION OF IRON-DEXTRAN COMPLEX ("FERON"). (E.) Haddow, A. (Chester Beatty Inst., London, S.W.3), F. J. C. Roe and J. V. Mitchley. *Brit. Med. J.* 1:1593-1594, 1964.

Random-bred rabbits (3 male, 3 female; approx. 1 year old) received i.m. inj. of iron-dextran complex (100 mg./wk. x 28), and sarcomas appeared at the site of inj. in 1 male at mo. 39 and in 1 female at mo. 48. The sarcoma-bearing female showed numerous pulmonary metastases and an adenocarcinoma of the mammary gland, probably of spontaneous origin. All 6 animals showed hepatic iron accumulation, necrosis, nodular regeneration and fibrosis. None of the s.c. or i.m. implants from the male sarcoma into 12 rabbits grew; none

of the implants from the female sarcoma into 4 cortisone-treated rabbits grew. Portions of the sarcoma from the female were grown in tissue culture; the occurrence of both micronuclei and large nuclei (possibly octaploid) in the same cells suggested chromosome non-disjunction, since no stages of amitotic division were seen.

64-1097 THE SPREAD FROM UNIFORMITY TO DIVERSITY WHEN BENIGN TUMORS BECOME MALIGNANT. (E.) Rous, P. (Rockefeller Inst., New York) and J. S. Henderson. *Am. J. Path.* 44(6):19a, 1964.

Comment is made on the diversity of cancer types derived from variously induced papillomas (Shope virus in rabbits, mouse bladder, mouse pulmonary adenomas). The same is true for the benign papillomas which appear on tarred mouse skin. After deep transplantation into young mice, these growths were no longer "conditional" tumors, requiring help to establish themselves on the skin, but grew steadily and proved fatal. Several have now been propagated in many successive hosts by repeated transfer and have remained unchanged, yet widely various cancers continue to take off from them.

64-1098 TUMORS IN EVANS RATS FED VEGETABLE OILS. (E., Abstract) Bryson, G. (Cottage Hosp., Santa Barbara, Cal.) and F. Bischoff. *Proc. Am. Assn. Cancer Res.* 5(1):8, 1964.

Groups of 30 female Evans rats reared on Purina Laboratory Chow (LC) were placed on special ad lib diets at 2 mo. of age for 20 mo. when the experiment was terminated. Those on 100% LC developed 5 mammary fibroplasias and 2 lymphoid tumors. A group on 90% LC + 10% USP cottonseed oil developed 3 mammary fibroplasias, 5 lymphoid tumors, 1 breast adenocarcinoma and 2 sarcomas. A group on 90% LC + 10% USP sesame oil developed 2 mammary fibroplasias, 2 lymphoid tumors, 4 breast adenocarcinomas, 1 fibrosarcoma (mammary), 1 pleomorphic sarcoma (neck) and 2 cellular sarcomas (uterus, mesentery). Differences between groups for mammary fibroplasia and lymphoid tumors were not significant. The 8 other neoplasms which developed in the sesame oil series as contrasted with zero in the controls indicate significance. No renal pigmentation bodies were found. (See also CRA 2(6):#1099, 1964.)

64-1099 TRIOLEIN AS A COCARCINOGEN. (E., Abstract) Bryson, G. (Cottage Hosp., Santa Barbara, Cal.) and F. Bischoff. *Fed. Proc.* 23(2) (Pt. 1):106, 1964.

When groups of 33 orchietomized male Marsh mice were given 6 β -hydroperoxy-4-cholesten-3-one (H; 5 mg s.c.) in sesame oil (SO) and H in triolein (TR), when observed to age 19 mo., 9% and 18% local sarcomas were produced, resp. No SO or TR controls developed tumors. In groups of 28 intact

BALB mice no local sarcomas were produced by s.c. inj. of 10 mg H but H in S0 produced 7% hemorrhagic cysts. In Marsh mice, lung adenomas were not increased by H (15%, controls, 9% and 15%); however, H in saline increased them to 39% in BALB mice (controls, 18% and 14%). To date, H in S0, cottonseed oil, and/or TR has produced local sarcomas in Marsh and C57 mice and in Evans rats, but none in Swiss and BALB mice. In saline, H has not produced local neoplasms in Marsh, BALB or Evans strains. When effective, TR, a major constituent of the oils tested, apparently acts as a local cocarcinogenic factor.

64-1100 CHROMOSOMAL ABERRATIONS INDUCED BY HYPO-NITRITE AND HYDROXYLAMINE DERIVATIVES.

(E.) Borenfreund, E. (Sloan Kettering Inst. Cancer Res., New York), M. Krim and A. Bendich. J. Nat. Cancer Inst. 32(3):667-679, 1964.

Fragmentations, translocations, and rearrangements of the metaphase chromosomes of mouse embryo and Chinese hamster cells were induced by N-methylhydroxylamine, N-hydroxyurethan, hydroxyurea, N-hydroxyaminoacetic acid, and hyponitrous acid. It is believed that these effects represent a direct attack on the DNA of the chromosomes since these agents induced main-chain cleavage of isolated DNA in soln.

64-1101 AGE AND BREED EFFECTS ON INDUCTION OF FIBROSARCOMAS BY DIBENZ[a,h]ANTHRACENE IN PIGEONS. (E.) Prichard, R. W. (Dept. Path., Bowman Gray Sch. Med., Winston-Salem, N. C.), J. W. Eubanks and C. C. Hazlett. J. Nat. Cancer Inst. 32(4):905-915, 1964.

A more extensive presentation of the paper abstracted as CRA 1(4):#696, 1963. Among the breeds tested, there was no correlation between tumor incidence and susceptibility to atherosclerosis.

64-1102 PITUITARY HORMONES AND LIVER CARCINOGENESIS WITH N-HYDROXY-N-2-FLUORENYL-ACETAMIDE. (E.) Weisburger, J. H. (NCI, Bethesda), S. R. Pai and R. S. Yamamoto. J. Nat. Cancer Inst. 32(4):881-904, 1964.

A more extensive presentation of the paper abstracted as CRA 1(11):#1900, 1964.

64-1103 PATHOGENESIS OF INDUCED BRAIN TUMORS IN MICE. (Rus.) Arkhangel'skii, V. V. (N. N. Burdenko Inst. Neurosurg., Acad. Med. Sci. USSR, Moscow). Vop. Neirokhir. 27(2):5-9, 1964.

Black C57 mice (total 143) received 1-2 crystals of 9,10-dimethyl-1,2-benzanthracene (DMBA) into the brain; histologic changes were studied from 1 hr. to 300 days after implantation. DMBA changed the course of the healing process in the

brain at an early stage; it also influenced leukocyte maturation and macrophage activity. Tumors developed in 20 mice, most of which showed mesenchymal structure. Among factors influencing the multiplication of the mesenchymal elements around DMBA crystals were trophic disturbances and repeated hemorrhages. The mesenchymal tumors in most cases were reticulum cell and spindle cell sarcomas.

64-1104 EXPERIMENTAL STUDY ON ANIMALS ON THE QUESTION OF FETAL DAMAGE BY PYRIMETHAMINE. (Ger.) Hickl, E. J. (1st Gynec. Clin. U. Munich, Germany), U. Mohr and G. Martius. Arch. Gynaek. 199(6):634-640, 1964.

Pyrimethamine (Daraprim), which appeared to have been involved in the sudden death of an infant whose mother received the drug at the end of the first trimester, was admin. intragastrically in doses ranging from 4-16 mg/kg/day to Sprague-Dawley rats during different periods of pregnancy (days 4 to term). Those rats which received the drug before implantation (day 7), showed 74.6% fetal resorptions (100% in those rats receiving 8 mg/kg/day); 2/15 fetuses carried to term showed malformations. Damage to the liver was not observed.

64-1105 BIOCHEMICAL AND HISTOCHEMICAL CHANGES IN EXPERIMENTAL HEPATOMA. (Fr.) Crăciun, É.-C. (Victor-Babes Inst. Pathol. Anat., Rumanian Acad. Sci., Bucharest), F. Motzoc, L. Georgescu and S. Constantinescu. Bull. Assn. Franc. Cancer 50(4):637-650, 1963.

The relationship between biochemical and morphological changes in liver tissue was studied in 200 male albino rats treated with p-dimethylamino azobenzene (DAB; 0.045 mg/kg/day for 14-19 mo.). Carcinogenesis progressed in 3 stages. Stage 1 (3-8 mo.) was characterized by intumescence and various types of nuclear damage, decrease in pyruvic, malic, and succinic dehydrogenase, and increase in aldolase and acid as well as alkaline phosphatase activity. Stage 2 (10-12 mo.) was characterized by marked epithelial polymorphism and adenoma formation, and further nuclear changes also increase in malic, pyruvic and succinic dehydrogenase (though not to normal levels) and decrease in aldolase and phosphatase activity. Stage 3 (14-19 mo.) was characterized by appearance of grossly visible carcinomas of the trabecular, adenomatous, or spinocellular type, decrease of dehydrogenase, phosphatase, and aldolase activity to a minimum at 14-15 mo., followed by a new increase. During the second and third stages, PAS-positive material in the sections decreased progressively, while DNA levels increased. The results indicate that experimental carcinogenesis involves slight but significant changes in the Krebs cycle which are paralleled by morphological and histochemical changes.

discussion is presented of methods of improving the situation by detoxification of the exhaust gases, redesign of automobiles so that the exhaust is not discharged so close to the ground where it becomes a special hazard to small children, maintenance of auto inspection to insure optimal operation of the motor as well as decreasing the air pollutants from industries and homes.

- 64-1111 APPLICATION OF THE TEST ON NEWTS (*TRITURUS CRISTATUS*) FOR QUICK DETECTION OF CARCINOGENIC PROPERTIES OF DYES. (E.) Krauze, S. (Dept. Foodstuff Commod. Res., State Inst. Hygiene, Warsaw, Poland), E. Stec and M. Młodecki. *Polish Med. J.* (5):789-797, 1963.

This article is the English version of a Polish article appearing in *Roczn. Panstw. Zakl. Hig.* 14(1-2), 1963. The carcinogenic properties of various dyes were studied in *T. cristatus* following s.c. inj. of their suspensions or soln. in olive oil (conc. = 0.1%). Of the azo dyes, fatty red, cochineal red and amaranth showed epithelial hyperplasia with infiltration of underlying tissue; Sudan G, acid yellow and alizarin showed no changes; the xanthene dyes, water eosin, uranine A and rhodamine B, caused epithelial hyperplasia without infiltration.

- 64-1112 REPORT OF THE YORKSHIRE COUNCIL OF THE BRITISH EMPIRE CANCER CAMPAIGN. (E.) Green, H. N. Pp. 467-478 in *British Empire Cancer Campaign* 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1., 707 pp., 1963.

A partial report of the activities of this council follows. Pretreatment with 9,10-dimethyl-1,2-benzanthracene of mice fed 4-ethylsulfonylnaphthalene-1-sulfonamide indicated the hyperplastic agent (HPA) was not a good promoter (see CRA 2(4):#668, 1964). G. M. Bonser and D. B. Clayson showed that the study of 17 analogs of HPA gave some insight into the molecular requirements for its hyperplastic action, which did not occur in studies made using bladder pouches rather than the intact bladder. P. F. Wilde showed that fractions of perfused livers from rats fed 50 mg of 3'-methyl-4-dimethylaminoazobenzene showed max. binding in the microsomes. In another study, J. O. Laws has shown that histological examination of livers from female Leeds rats subjected to partial hepatectomy after feedings of 2-acetylaminofluorene (AAF) for 3 or 8 wk., revealed severe delay and distortion of the regeneration process. Hepatectomy did not influence regeneration when ethionine was administered to Leeds male rats, indicating a different type

of action. P. K. Goswami has shown that local eosinophilia appeared in C57BL mice 30 days after s.c. inj. of methylcholanthrene (MC; 0.1 ml of 0.2% soln.) and tricycloquinazoline (TCQ; 1 mg); TCQ produced the greater response. Inj. of isolated liver cells from an animal having received TCQ also produced a local eosinophil leukocyte reaction in an isologous host. In another study, when the draining lymph nodes were taken from C57BL mice immunized against an A strain spontaneous mammary carcinoma and a suspension inj. into (A + C57BL)F1 hybrid mice, the number of takes of s.c. grafts of the same tumor was decreased in treated animals.

- 64-1113 TUMOR-PROMOTING POWER AND HYPERPLASIA-INDUCING POWER OF A NUMBER OF IRRITANT SOLUTIONS. (E., Abstract) Frei, J. V. (Dept. Path., McGill U., Montreal, Canada) and A. C. Ritchie. *Fed. Proc.* 23(2)(Pt.1):288, 1964.

A study of tumor promotion by 10 irritant soln. on mouse skin pretreated once with a carcinogen showed greatest effect (in decreasing order) from 5% croton oil, 100% Tween 60, and 100% toluene. The same 3 soln., in the same decreasing order, induced earlier and more sustained epidermal hyperplasia than the other soln. investigated. When 3 different conc. of croton oil were employed a similar relationship between promoting power and power to induce hyperplasia was seen.

- 64-1114 PATHOLOGY OF CYCAD TOXICITY IN ANIMALS. (E., Abstract) Muger, G. M. (Michigan State U., East Lansing), C. K. Whitehair and O. Mickelsen. *Fed. Proc.* 23(2)(Pt.1):106, 1964.

Rats fed 2% cycad nut meal in a natural grain ration for 160 days developed benign adenomas, hepatomas and hyperplastic gastroenteritis. The same diet during gestation produced young with massive necrotic hepatitis and alveolar hemorrhages of the lungs. Lesions of cystic papillary tubules and marked proliferation of tubular epithelium, forming cell cords suggestive of early adenoma formation, occurred in the sow on a 2% cycad diet. Similar, but more marked changes arose in pig and cow sucklings of parents on this diet for 3 mo. (See also CRA 1(11):#1931, 1964.)

- 64-1115 BRONCHO-PULMONARY CANCER AND ARSENIC POISONING IN WINEGROWERS OF BEAUJOLAIS (Fr., Abstract) Latarjet, (Ed.-Herriot Hosp., Lyon, France), Galy, Maret and Gallois. *Mem. Acad. Chir. (Paris)* 90(13-14):384-390, 1964.

See CRA 1(12):#2202, 1964.

See also abstract no.: 1019

VIRAL CARCINOGENESIS

64-1116 BIOLOGICAL AND BIOCHEMICAL HETEROGENEITY OF ROUS SARCOMA VIRUS PREPARATIONS. (E., Abstract) Ph.D. Thesis, U. Microfilms, Inc., Ann Arbor, No. 64-1174). Righthand, V. F. (Rutgers Univ., New Brunswick, N. J.). Dissertation Abstr. 7(7):2662-2663, 1964.

Rous sarcoma virus (RSV) preparations made from virus-infected brain tissue of chicks were demonstrated to be heterogeneous by extraction (by means of a modified Hughes' press) and differential centrifugation (which removed 99.99% of the infectivity). The non-sedimentable fractions had oncogenic potency (comparable to 230 ED₅₀ U standard RSV preparations) which was partially inhibited by RNase, streptomycin and protamine, but not by DNase and trypsin. Fibrillar material which was partially chemically characterized was also obtained from this fraction which when inoculated s.c. caused a high incidence of bilateral, extensive kidney lesions (with proliferative, epithelial foci) in the absence of wing web tumors. Fractions from infected tissue, uninfected tissue or standard RSV preparations did not induce these lesions.

64-1117 STUDIES ON THE VIROLOGY AND TRANSPLANTABILITY OF REGRESSING ROUS SARCOMA. (E., Abstract) Dinowitz, M. (Dept. Microbiol., Johns Hopkins U., Baltimore, Md.) and H. Rabin. Bact. Proc. 1964:134.

Rous sarcoma virus (RSV)-induced tumors were assayed for 2 days, 7 assays in chick embryos and the tumor extracts and the tissue culture fluid (TCF) of tumor explants revealed no virus. On another occasion, the TCF of 2 other such tumors had a low virus titer (60-100 infectious units/ml). No virus was found after challenging tissue cultures of 4 of these tumors with RSV. When passaged on the chick chorioallantoic membrane (CAM), 2 of these tumors yielded high virus titers by passage 3; 3 other tumors failed to pass in this manner and did not yield virus. RSV was found initially in 3 progressively regressing tumors but all 3 passaged successfully on the CAM and the first passage tumors yielded high virus titers. The inability to detect RSV in some of these tumors is not clear but may be due to an interfering agent.

64-1118 UTILIZATION OF GLUCOSE AND FRUCTOSE BY ROUS SARCOMA VIRUS INDUCED TUMORS. (Abstract) Ahmed, M. (Dept. Microbiol., Indiana U. Sch. Med., Indianapolis) and A. S. Saks. Fed. Proc. 23(2)(Pt. 1):132, 1964.

Rous sarcoma virus-induced tumors of 10-12-day old chick chorioallantoic membranes (CAM) were incubated for 3 hr. with glucose (G) and/or fructose (F), 3 times as much G was utilized by tumors as by CAM. F did not inhibit G uptake by

tumor; however, F inhibited G uptake by CAM. Uptake of F by tumor was markedly reduced by the presence of G; this effect was not observed with CAM.

64-1119 MORPHOLOGICAL DISTINCTION OF TYPE B VIRUS PARTICLES IN MAMMARY TUMORS OF STRAIN A MICE. (E.) Hairstone, M. A. (Rockefeller Inst., New York), M. J. Lyons and D. H. Moore. Virology 23(2):294-297, 1964.

Electron micrographs made from mammary tumor tissue (both external and internal) from Strain A and Strain III mice, showed a distinct profile of Type B virus particles for each strain. In Strain A, the nucleoid was larger and of a different structure and density than that in Strain III. A comparison of negatively stained particles from the milk of these 2 strains, also portrayed patterns unique to each strain. A possible relationship between these morphological differences and the difference in tumor development seen in each strain is discussed.

64-1120 AGAR SUSPENSION CULTURE FOR THE SELECTIVE ASSAY OF CELLS TRANSFORMED BY POLYOMA VIRUS. (E.) Macpherson, I. (Inst. Virol., U. Glasgow, Scotland) and L. Montagnier. Virology 23(2):291-294, 1964.

Polyoma-transformed clones derived from BHK 21/13 hamster cells were selectively assayed by plating the cells in a soft agar medium. Using this method, the transformation dose-response curve (PFU/cell against colonies/10⁵ cells) was linear over a range of 1-500 PFU with a log slope of 1. The transformation rate is 3-5 times higher than that obtained on glass. The selectivity toward cells transformed by polyoma virus was demonstrated by the fact that uninfected BHK 21/13 cells and hamster embryo cells derived from primary to fifth passage cultures did not form colonies when 10⁵ to 5 x 10⁵ cells were plated in the agar medium.

64-1121 EFFECT OF ROUS SARCOMA VIRUS ON CULTURES OF NORMAL HUMAN FIBROBLASTS. (E., Abstract) Girardi, A. J. (Wistar Inst., Philadelphia, Pa.), F. C. Jensen and H. Koprowski. Fed. Proc. 23(2)(Pt. 1):401, 1964.

When actively proliferating cultures of human fetal diploid cell strains (HDCS) were exposed to tumor extracts of the Schmidt-Ruppin strain for 7 days, foci of altered cells with vacuolated or granular cytoplasm and enlarged nuclei with chromatin aggregates were observed. The foci formed by altered cells were not typical, but a cytopathological effect (CPE) was seen in localized areas of the monolayer. Exposure of cell cultures nearing the end of their finite life (Phase III),

produced larger aggregates of altered cells, following increased mitotic activity. Cells of adult human buccal mucosa, lacking a small acrocentric chromosome, were highly susceptible to the CPE of Rous tumor extracts and the supernatant of these cultures produced more pronounced changes in Phase III of HDGS cultures.

- 64-1122 PROPAGATION OF A SIMIAN TUMOR AGENT (YABA VIRUS) IN CULTURES OF HUMAN AND SIMIAN RENAL CELLS AS DETECTED BY IMMUNOFLOUORESCENCE. (E.) Levinthal, J. M. (Dept. Bact., Harvard Sch. Med., Boston, Mass.) and H. M. Shein. *Virology* 23(2):268-271, 1964.

Using fluorescein-labeled goat anti-monkey globulin and anti-Yaba rhesus monkey serum, an immunofluorescence stain can be obtained to monitor the propagation of simian poxvirus Yaba-induced tumor cells in monolayer cultures of human fetal kidney cells (HFK) and grivet monkey kidney (GMK) cultures. Specific viral antigen was detected in a total of 12 GMK cultures during 3 serial passages of Yaba and in 19 HFK cultures during 6 serial passages of the virus over an interval of 9 mo. The morphology and distribution of specific immunofluorescence were similar in the 2 tissues, but the proportion of cells with specific viral antigen and the intensity of stain was less in HFK. This method proved more sensitive than detection by cytopathic effect and more convenient than bioassay methods.

- 64-1123 CONTINUOUS CULTIVATION IN VITRO OF FRIEND VIRUS (FV) INDUCED ASCITES TUMOR. (E., Abstract) Fieldsteel, A. H. (Stanford Res. Inst., Menlo Park, Cal.), P. J. Dawson and W. L. Bostick. *Fed. Proc.* 23(2)(Pt. 1):131, 1964.

An FV-induced reticulum cell sarcoma (originally in BALB/c mice as an ascites tumor) maintained through 21 generations in tissue culture (TC) has retained its lymphoid-like morphology and cells from all passages have produced typical ascites and metastases *in vivo*. However, the number of cells required to produce ascites was at least 2×10^4 TC from passage 12 compared to 3.4×10^2 cells of the original tumor. When examined for virus, both the original tumor cells and the TC cells showed less than 1 ID₅₀ of cell-associated FV/10⁶ cells. However, the cell-free ascitic fluid from the tumor contained 10^{3.1} ID₅₀/ml, compared to barely detectable FV in undiluted TC fluid.

- 64-1124 CELL TRANSFORMATION IN VITRO AND TUMOR INDUCTION IN VIVO BY LARGE- AND SMALL-PLAQUE POLYOMA VIRUS. (E.) Diamond, L. (Wistar Inst., Philadelphia, Pa.). *Virology* 23(1):73-80, 1964.

In the first of two experiments, cultures of primary and secondary mouse embryo cells (obtained from a culture of whole mouse embryo) and

hamster kidney cells (obtained from a clone of BHK21 cells) were exposed to large-plaque and small-plaque polyoma virus suspensions to determine the percent of cell transformation; in the second of the experiments, newborn Syrian hamsters (less than 48 hr. old) were inoc. i.p. or s.c. with 0.03 ml of the polyoma virus suspension, killed 6 days after inoc. and the gross pathology was recorded. Large-plaque and small-plaque polyoma virus suspensions were found to transform the same percentage of hamster kidney cells *in vitro* when similar exposure multiplicities were used. Measurements on the adsorbed multiplicities showed that more small-plaque than large-plaque virus actually adsorbed to the cells, and, therefore, that more transformed colonies per adsorbed hemagglutinin or plaque-forming unit were produced by large-plaque virus suspensions than by small-plaque. A high proportion of kidney tumors and few peritoneal tumors were induced by large-plaque virus suspensions in newborn hamsters, while reversal in anatomic site frequency was seen with small-plaque suspensions. A difference in the adsorption qualities of the two plaque types may explain the difference in tumor site incidence.

- 64-1125 CATTLE LEUKOSES AND HUMAN LYMPHADENOSES: A PRELIMINARY REPORT. (E.) Aleksandrowicz, J. (3rd Clin. Int. Dis., Cracow Med. Acad., Poland), A. Wolska and T. Szuperski. *Texas Rep. Biol. Med.* 22(1):3-8, 1964.

Leukograms made from the blood of 2,000 cattle destined for slaughter presented 22 leukemia-like cases (lymphocytosis greater than 75%). Lymphadenopathy was not confirmed in 1 animal. Using this hematological examination rather than gross examination of the carcasses, the percentage of animals diagnosed as leukemic increased 30-fold. In a second study, 12 of 3,000 cows (age 5-10 yr) presented blood pictures with 90% lymphocytosis; 10 had been suspected on gross examination and, with 6, lymphadenosis was confirmed histopathologically. In this study, the percentage of animals diagnosed was increased 10-fold by using the hematological examination. Although there is no proof of viral infection from animal to man, statistics show a correlation of the index of human morbidity from leukemia and the amount of meat consumed by the population, which, in the author's opinion, is evidence enough to merit the introduction of hematological studies in the examination of cattle for slaughter.

- 64-1126 IMMUNOGENESIS AND LEUKEMOGENESIS: EXPERIMENTAL AND CLINICAL ASSOCIATIONS. (E., Abstract) Peterson, R. D. A. (Dept. Pediat. U. Minnesota, Minneapolis) and R. A. Good. *Fed. Proc.* 23(2)(Pt. 1):189, 1964.

Several experimental and clinical studies suggest a close association between development of the immune system and development of lymphoreticular malignancies. While the dual role of the mouse

thymus in immunogenesis and leukemogenesis is well established, recently a similar dual role was shown for the chicken's bursa of Fabricius (see CRA 1(11):#1978, 1964). Early involvement of the immune system in mice by passage A virus is demonstrated by decreased antibody forming capacity (see CRA 1(11):#1947, 1964). Clinically an immunologic deficiency was found in a syndrome which included ataxia, telangiectasia, lymphoreticular malignancies and an abnormal thymus (see CRA 2(6):#1127, 1964). These observations suggest to us that malignancies of the lymphoid system are due to disturbances of lymphoid differentiation whether viral-induced or genetically conditioned. The same abnormality may also affect the immune system.

4-1127 ATAXIA-TELANGIECTASIA. ITS ASSOCIATION WITH A DEFECTIVE THYMUS, IMMUNOLOGICAL-DEFICIENCY DISEASE, AND MALIGNANCY. (E.) Peterson, R. D. A. (Variety Club Heart Hosp., Minneapolis, Minn.), W. D. Kelly and R. A. Good. *Cancer* 1:1189-1193, 1964.

4 of 6 pts. with ataxia-telangiectasia (5 female, including 2 pairs of sisters, age 3-11 and male age 3), the lymph node structure was abnormal: 2 showed reticular cell hyperplasia and showed decreased cellularity of the germinal centers. At necropsy 1 pt. was found to have had lymphosarcoma and another reticuloendotheliosis. The cellular and serological aspects of the immune system were studied in several of these pts.; one showed no plasma cells in an otherwise normal bone marrow while in another plasma cells were rare. Serum-immunoglobulins were also studied; 4/5 showed absent or low γ . One case showed a total absence of γ -globulin. The thymus appeared to be absent in 3 cases and small in another case.

4-1128 STUDY ON CAUSAL AGENT OF HUMAN LARYNGEAL PAPILLOMA. (E.) Kasahara, S. (Kitasato Inst., Tokyo), I. Yoshioka, M. Itoh and S. Ohshima. *Kitasato Arch. Exp. Med.* 33(1-4): 44, 1960.

All fragments of laryngeal papillomas from 6 young pts. when transplanted onto chick chorio-allantoic membranes (CAM) developed pocks. When autopsy specimens (from 4 pts.) were introduced into the anterior chamber of a guinea pig's eye, produced a tumor. Histopathological changes of the tumor were clearly papillomatous.

4-1129 CELLULAR INJURY BY POLYOMA VIRUS. (E., Abstract) Kirsten, W. H. (Chicago, Ill.), D. A. Kindig and B. Spargo. *J. Path.* 44(6):26a, 1964.

earliest electron microscopic evidence of polyoma virus (PV) multiplication in various

embryonal cells was found in the nucleus 12 hr. after infection. Complete virus particles were seen first around the nucleolus or near the nuclear membrane; there was also clumping of the nucleolone and progressive loss of chromatin. PV was then released from the nucleus into the cytoplasm as free or membrane-bound particles. Typical cytopathic effects and death followed.

64-1130 EFFECTS OF ACTINOMYCIN D AND OF MITOMYCIN C ON THE DEVELOPMENT OF ROUS SARCOMA VIRUS. (E.) Vigier, P. (Pasteur Lab., Radium Inst., Paris) and A. Goldé. *Virology* 23(4):511-519, 1964.

The addition of low conc. of actinomycin D (AD; 0.1 μ g/ml of medium) 4 hr. before to 5 hr. after infection of secondary cultures of chick embryo cells with Rous sarcoma virus (RSV) caused complete and irreversible arrest of cell growth; during this period RSV production was inhibited 10-20-fold. RSV inhibition was much less when AD was added after 18 hr. and insignificant and reversible 48 hr. after infection. A higher conc. of AD (1 μ g/ml) was required to stop cell growth completely when added 48 hr. after infection. The addition of mitomycin C (MC; 1 μ g/ml) arrested cell growth completely at all times. MC inhibited RSV production only when added within 24 hr. after infection and its action was irreversible. Results suggest that at least two DNA-dependent events are required for the development of RSV.

64-1131 IRREVERSIBLE PHOTOSENSITIZATION OF VIRUSES. (E.) Wallis, C. (Dept. Virol., Baylor U. Coll. Med., Houston, Texas) and J. L. Melnick. *Virology* 23(4):520-527, 1964.

Among a group of 7 viruses, only herpes and measles viruses were completely photosensitive to 10^{-4} M conc. of neutral red (NR), proflavine (P) or toluidine blue (TB) when incub. under ideal conditions (pH 9, 37°C). SV40, parainfluenza and vaccinia viruses were photosensitized only by TB, while the reo-virus and influenza virus were completely photosensitized by TB or P. No photosensitization of picornavirus under these conditions was noted. Adenoviruses were not completely photosensitized by NR or P and were inactivated in the dark by TB.

64-1132 ONCOGENICITY OF TWO STRAINS OF CHICKEN SARCOMA VIRUS FOR RATS. (E.) Munroe, J. S. (Sloan-Kettering Inst. Cancer Res., New York) and C. M. Southam. *J. Nat. Cancer Inst.* 32(3): 591-623, 1964.

Of 102 Wistar and Sprague-Dawley rats, inoc. s.c. or i.p. when newborn, with the Bryan strain of Rous chicken sarcoma virus (B-RSV; 20% tissue mince), only 1 developed a solid tumor. Of 221 rats inoc. s.c. or i.p. when 5-6 wk. old, without

or with conditioning (X-rays and/or i.m. cortisone, and 20-methylcholanthrene), 6 developed solid tumors in the cervical, axillary, or inguinal region. After inj. of B-RSV, virus was not demonstrated in any of these tumors. When the Carr-Zilber strain of chicken sarcoma was inj. (CZ-RSV; same dosage and methods as with B-RSV) into 162 7-day-old rats, 73 developed cystic hemorrhagic tumors in the cervical, axillary and inguinal regions, and 4 developed solid tumors at the site of previous cystic tumors. When rats were inoc. at 2-6 wk. of age, no cystic tumors developed, but solid tumors appeared in 5/45 rats given inj. of the material at this age. Up to 11 wk. after inoc., infective virus was demonstrated in the capsule of some cysts, but older cysts and tumors yielded no virus. Neutralization studies indicated that these two strains of chicken sarcoma virus were antigenically dissimilar.

- 64-1133 IN VITRO CULTURE OF PULMONARY TUMORS PRODUCED IN THE HAMSTER BY ADENOVIRUS 12. (Fr.) Barski, G. (Gustave-Roussy Inst., Villejuif/Seine, France) and F. Cornefert. Ann. Inst. Pasteur 107(1):109-114, 1964.

Newborn golden hamsters were inoc. intrathoracically with approx. 10^4 ID₅₀ of adenovirus (AD) 12, Strain HUIE. After 1 1/2-3 mo. 16/22 had dedifferentiated carcinomas which, upon histologic examination, revealed their bronchiolar-alveolar origin. Five of these tumors were transplanted s.c. or in the cheek pouch of golden hamsters (aged 1-3 mo.), and then transferred to tissue cultures consisting of a synthetic medium, NCTC 109, to which 15-30% veal serum had been added; 4 of the tumors were transferred directly to the tissue culture. During consecutive passages in vitro, the cultures showed a tendency to become purely epithelial. The cells had a peculiar morphology, with hypertrophic, interphasic nuclei which contained extra chromatin. The cultures retained their malignant properties, producing tumors similar to the primary ones upon re-inoculation into hamsters. AD 12 was not found in the tumor cultures; seroneutralizing antibodies were not detected in tumor-bearing animals. The cultures were resistant to a superinfection with AD 12, but not with AD 5 which was used for comparison; this finding is difficult to interpret, as a similar resistance was observed in normal lung tissue cultures of the hamster.

- 64-1134 KARYOLOGICAL CHARACTERISTICS OF PULMONARY TUMORS PRODUCED IN HAMSTERS BY ADENOVIRUS 12. (Fr.) Barski, G. (Gustave-Roussy Inst., Villejuif/Seine, France) and F. Cornefert. Ann. Inst. Pasteur 107(1):114-120, 1964.

In continuation of the work described in the preceding abstract, karyological analyses were carried out on 2 of the primary tumors after 5 and 7 in vitro passages, and on 2 of the transplanted

tumors after their first passage in vitro. One of the primary tumors had become purely epithelial during in vitro passage, while the other 3 were of mixed composition, containing fibroblasts, macrophages, and epithelial islets. In all cases, mitoses with the normal number of chromosomes (44) were predominant. Close inspection revealed, however, that the apparently normal mitoses often showed pseudo-diploidy or pseudo-tetraploidy or other abnormalities, which affected autosomes as well as X-chromosomes; chromosomal lesions, such as fragmentation or double constriction, also occurred quite frequently. These changes were not considered typical or specific, as they followed no discernible pattern. Starting with the first in vitro passage, the tumor cells showed a relatively high percentage (8-33%) of polyploid mitoses; these cells showed no tendency to accumulate in the course of successive passages.

- 64-1135 THE PATHOLOGICAL MORPHOLOGY OF VIRUS-INDUCED (SV40) NEOPLASMS IN NEWBORN GOLDEN HAMSTERS. II. HYPERPLASIA AND PAPILLOMA OF THE CHOROID PLEXUS OF THE CEREBRAL VENTRICLES AFTER SUBCUTANEOUS OR INTRAMUSCULAR INJECTION OF THE VIRUS. (Ger.) Unterharnscheidt, F. (German Res. Inst. Psychiat., Max Planck Inst., Munich, Germany), O. Bonin, K. Schmidt and I. Schmidt. Acta Neuropath. (Berlin) 3(4):362-371, 1964.

In 35 golden hamsters which had received s.c. or i.m. inj. of SV40 virus [titer = $102.0-107.5$ dim/ml (unit as given in paper)] at the age of 1 day and were sacrificed 13 mo. later, tumors of the body were found in one. However, serial sections of the brain and spinal cord of the others showed changes in the choroid plexus. The choroid plexus varied in appearance from histologically normal tissue through more or less hyperplasia to tumor-like formations in the remainder. In 12 of the animals, attenuated polio virus was inj. with the SV40 and all showed changes in the choroid plexus. The central nervous system of the hamster which showed a body tumor was not examined; all the others showed some degree of hyperplasia of the choroid plexus.

- 64-1136 TUMOR PREVENTION IN HAMSTERS INFECTED WITH SV40 VIRUS. (Rus.) Deichman, G. I. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and T. E. Kliuchareva. Vestn. Akad. Med. Nauk SSSR 19(6):72-75, 1964.

When SV40 was admin. to newborn (0.2 ml; 10^5 or 10^7 TID₅₀) or adult (0.5 ml; 10^7 TID₅₀) hamsters, no tumors appeared when they were reinfected with SV40 during the latent period, or when re-infection with SV40 was combined with immunization by the corresponding tumor cells. Immunization of hamsters toward the end of the latent period decreased the frequency of tumor formation. Immunization at the time the first tumor appeared or later had no effect on tumor frequency, compared with that in controls.

64-1137 LEUKEMIA OF CATTLE. (Ger., Abstract)
Mitscherlich, E. *Klin. Wschr.*
42(12):601, 1964.

For the regions where cattle are affected by leukemia, the phases of the disease, and the characteristic necropsy findings are described. This disease causes tremendous losses in central Germany. The leukemia is transferred to calves via the placenta and milk. It is transferable by cell-free preparations. Inclusion bodies and elementary forms have been seen in leukemic cells; antibodies and virus-like particles have been shown in blood of affected animals, and their numbers are correlated statistically with the absolute lymphocyte count. Characteristic kidney and liver changes were observed after inoc. of white NMRI mice. Furthermore, 3-22 days after inoc., a hemolyzing substance was found in the spleen and liver of mice. In a neutralization test, the appearance of this substance could be prevented by pretreatment of the infectious material *in vitro* by the serum of a leukemic cow and that of a pt. with Hodgkin's disease. In control animals inj. with the same infectious material pretreated *in vitro* only with physiological saline, the hemolyzing substance was again found.

64-1138 PATHOLOGIC MORPHOLOGY OF VIRUS-INDUCED (SV40) NEOPLASMS OF NEWBORN GOLDEN HAMSTERS. PART I: POLYMORPHOCYLLULAR SARCOMA OF THE SUBCUTANEOUS CONNECTIVE TISSUE AND MUSCULATURE IN THE AREA OF THE SITE OF INJECTION. (Fr.) Bonin, O. (Paul-Ehrlich Inst. Exptl. Med., Frankfurt/Main, Germany), Unterharnscheidt, I. Schmidt and K. Schmidt. *Z. Neuropath.* (Berlin) 3(4):351-361, 1964.

Various tissue culture extracts were inj. s.c. and/or i.m. into 1-day-old golden hamsters. With 21-day-old Rhesus kidney culture extract (RKCE; estimated SV40 virus titer = $10^{7.5}/\text{ml}$), tumors occurred in 10/28 hamsters within 6-12 mo. With 7-day-old RKCE (SV40 virus titer = $10^2/\text{ml}$), 4 developed a tumor in the 11th mo. With a conc. attenuated poliovirus from Rhesus kidney culture (SV40 virus titer = $10^{4.5}/\text{ml}$), tumors occurred in 9/28 within 10-13 mo. No tumors occurred after inj. of various preparations which lacked detectable SV40: a 21 day old Cercopithecus kidney culture (CKC); an attenuated poliovirus from CKC; a conc. of 5 different inactivated polio inoculas. It was concluded that tumors appear only after inj. of high doses of SV40 virus and only at the site of inj. The rate of tumor incidence also depended on SV40 dosage. These results suggested a direct carcinogenic or a stimulating effect of the SV40 viral material on the tissue. Tumors the size of chicken eggs were produced. The tumors were polymorphic, with spindle cell and round cell formations, with enormous giant cells and pronounced mitotic figures. The tumors were encapsulated and contained numerous necrotic areas (due to

cyanosis caused by rapid growth and encapsulation).

64-1139 THE INHIBITING ACTION OF IRRADIATED ISOLOGOUS LEUKEMIC EXTRACTS ON SPONTANEOUS LEUKEMOGENESIS IN AKR MICE. (Fr.) Latarjet, R. (Dept. Radiobiol., Pasteur Inst., Paris). *Ann. Inst. Pasteur* 107(1):1-26, 1964.

When newborn AKR mice were inj. (at unspecified intervals) with irradiated cellfree extracts (0.05 ml s.c. on day of birth, then 0.1 ml s.c., then 0.1 ml i.p., then 0.2 ml i.p. from inj. 4 on; total 1.25 ml in 8 inj.) prepared from ganglionic, thymic and splenic tissue of AKR mice with leukemia, a decrease in the incidence of spontaneous leukemia was noted if the irradiation dose was high enough to suppress the superinfection effect of the extract. Extracts of normal tissue were ineffective. Of 5 extracts irradiated with UV rays (30-40 k ergs mm^{-2}), one was inactive and the remaining 4 decreased the incidence of leukemia by 12-28%. X-rayed extracts (100 kr; indirect effect) were more effective, decreasing the incidence by 30-42%. The direct effect of X-rays (160 kr) yielded inactive extracts. UV-irradiated extracts (0.1-0.2 ml i.p. x 7; UV dose = 40 k ergs mm^{-2}) were found to decrease leukemia incidence by 28% after 250 days, even under conditions when sufficient active virus was present to cause superinfection. (See also CRA 2(2):#192, 1964.)

64-1140 MORPHOLOGY OF SHOPE PAPILLOMA VIRUS ASSOCIATED WITH NUCLEIC ACID-INDUCED TUMORS OF COTTONTAIL RABBITS. (E.) Chambers, V. C. (Dept. Microbiol., U. Washington Sch. Med., Seattle) and Y. Ito. *Virology* 23(3):434-436, 1964.

DNA (80-500 $\mu\text{g}/\text{ml}$ aqueous soln.) extract of Shope papillomas inoc. (0.1 ml of extract, intradermally) into 4 cottontail rabbits produced in 22/24 inoc. sites tumors that were grossly and microscopically the same as papillomas induced by intact virus. DNA-induced papillomas observed by electron microscopy contained typical virus particles with infectivity titers (based on 100% end point) of 10^{-2} - 10^{-3} .

64-1141 THE FATE OF POLYOMA VIRUS IN HAMSTER, MOUSE, AND HUMAN CELLS. (E.) Bourgaux, P. (Bacteriol. Lab., Free U. Brussels, Belgium). *Virology* 23(1):46-55, 1964.

A study was made of the interactions of hamster, mouse, and human tissue culture cells (HEP 2) with P32-labeled polyoma virus. Approx. one-third of the radioactive material that became attached and probably entered the cytoplasm of the cells was degraded within the 24 hr. following infection and appeared in the medium as acid-soluble material. Most of the radioactivity remaining acid-insoluble retained the physical characteristics of intact virus particles and was lost from the cytoplasm either by rejection into the medium or

by association with the nuclear fraction. In hamster cells the nuclear-associated radioactivity remained constant for at least 4 and probably 6 days, while the cells were actively dividing. To determine whether the persistence of radioactivity was due to the presence of virus particles, hamster cells, after exposure to radioactive virus, were mixed with a suspension of non-radioactive virus. Three days after infection, a significant amount of the radioactivity extracted banded in the same position as "full" virus particles in a rubidium chloride gradient.

64-1142 AN IMMUNOLOGICAL TEST FOR DEMONSTRATING SV 40 VIRUS. (E.) Chumakova, M. Ia.

Inst. Poliomyel. Vir. Encephal., Acad. Med. Sci. USSR, Moscow), M. P. Chumakov, T. I. Zavodova and S. G. Dzagurov. *Acta Virol.* 8(1):90-91, 1964.

When Wistar rats were given i.m. doses of SV40, 10^3 - 10^7 PFU in combination with i.m. adjuvant (1 part lanolin and 9 parts paraffin oil) antibody titer reciprocal (ATR) detected after 10 days was >8 ; when 3 doses of virus were given without adjuvant, ATR, detected at day 14 was >8 in 1/2 tests with 5×10^6 PFU and <4 in the other test and in one with 5×10^1 PFU. In guinea pigs given 1.5×10^4 - 10^7 PFU, i.p., plus adjuvant, antibody was detected at day 10 and was >8 . Immunological tests in rats fully agreed with virus isolation experiments in *Cercopithecus aethiops*. When minimal amounts of SV40 were present, they could only be demonstrated in the second passage of monkey kidney tissue cultures (over a period of 48 days) while specific neutralizing antibodies in rats could be demonstrated as early as 10 days after inoc. of the same virus preparation.

64-1143 ELECTRON MICROGRAPHS OF WOUND-TUMOR VIRUS IN AN ANIMAL HOST AND IN A PLANT TUMOR. (E.) Shikata, E. (Boyce Thompson Inst. Plant Res., Yonkers, N. Y.), S. W. Orenski, H. Hirumi, J. Mitsuhashi and K. Maramorosch. *Virology* 23(3):441-444, 1964.

Electron micrographs are presented of wound-tumor virus *in situ* in fat-body tissue sections of viruliferous leafhopper (*Agallia constricta*) and in sections of tumor cells from a diseased sweet clover plant (*Melilotus alba*). The insects had been restricted to a diet of wound-tumor diseased sweet clover plants for 4 wk. Clusters of uniform, dense, spherical particles (35-45 mμ in

diameter) were found exclusively in the cytoplasm of the fat-body cells. These were also frequently seen in plant stem tumors, but were never detected in normal plant tissues or in virus-free leafhoppers. Evidence seems to indicate that the dense particles found scattered or accumulated in tissue sections of wound-tumor-infected animals and in virus tumors of plants, are particles of the wound-tumor virus.

64-1144 THE EFFECT OF SIMIAN 40 VIRUS-INDUCED TUMOR ON THE ANTIGENIC BEHAVIOR OF HAMSTER SERUM. (Fr.) Dufour, D. (Dept. Biochem., Fac. Med., U. Laval, Quebec, Canada). *Laval Med.* 35(2):137-139, 1964.

A primary tumor obtained from hamsters inoc. with SV40 was in turn inoc. into 3 rabbits for the purpose of analyzing the immune serum. Antigenic modifications were observed in the serum of SV40 tumor-bearing hamsters. Immunoelectrophoretic studies revealed an alteration at the albumin level.

64-1145 AN AVIAN LEUCOSIS GROUP-SPECIFIC COMPLEMENT FIXATION REACTION. APPLICATION FOR THE DETECTION AND ASSAY OF NON-CYTOPATHOGENIC LEUCOSIS VIRUSES. (E.) Sarma, P. S. (NIH, Bethesda), H. C. Turner and R. J. Huebner. *Virology* 23(3):313-321, 1964.

A complement fixation test (COFAL test) which has some advantages over the resistance-inducing factor interference procedure was designed to detect and assay viruses of the avian leukosis group. Details of the assay are presented. Virus diluted 10^{-4} - 10^{-5} was detected within 10 days of virus inoc. and final titration end points were often reached within 2 wk. Rous associated virus was readily demonstrated in the Bryan strain but not in the S-R strain of Rous sarcoma virus. (See also CRA 2(5):#940, 1964.)

64-1146 EFFECT OF BURSECTOMY AND THYMECTOMY ON THE DEVELOPMENT OF VISCERAL LYMPHOMATOSIS IN THE CHICKEN. (E.) Peterson, R. D. A. (Pediat. Res. Lab., U. Minnesota, Minneapolis), B. R. Burmester, T. N. Fredrickson, H. G. Purchase and R. A. Good. *J. Nat. Cancer Inst.* 32(6):1343-1354, 1964.

A more extensive presentation of the paper abstracted as CRA 1(11):#1978, 1964.

See also abstract nos.: 1049, 1069, 1097, 1206, 1209

EPIDEMIOLOGY AND BIOMETRY

- 64-1147 MEMORANDUM ON RECENT STUDIES. IX. CHARACTERISTICS OF CARCINOMA OF THE UTERUS. (Jap.) Ando, K. (Dept. Obstet. Gynec., Keio U. Sch. Med., Japan). Sanka To Fujinka (Obstet. Gynec., Tokyo) 30(4):469-473, 1963.

The relative incidences of carcinomas of the cervix and of the uterus are generally 90% and 10%, resp. Carcinoma of the cervix is encountered more frequently among married women who have borne children (the incidence in nulliparas was only 10%) and also appeared at an earlier age. Carcinoma of the uterus among nulliparas represented 33% of all cases of carcinoma of the uterus. Carcinoma of the uterus is often accompanied by abnormal proliferations of other membranes of the body such as cystic glandular hyperplasia, feminizing ovarian tumor, granulosa or theca cell tumors. It is suggested that the stimulating action of estrogens contributes to the development of abnormal endometrial proliferation, and that the high incidences of excessive fat accumulation, hypertension, hirsutism, and diabetes among pts. with carcinoma of the uterus support the presence of adrenocortical hyperfunction or estrogen-progesterone imbalance.

- 64-1148 PRECANCEROUS STATES OF THE LARYNX. (Pol.) Włodyka, J. (Clin. Otolaryn., Acad. Med. Cracow, Poland). Pol. Tyg. Lek. 19(3):91-94, 1964.

The clinical and histologic studies on 1,061 diagnosed and treated cases of laryngeal cancer and 921 cases of laryngeal cornification (pachydermia, leukoplakia, keratosis, hyperkeratosis), chronic inflammations, cysts, benign tumors and proliferative changes including polyps, are presented. Cornification was found in 135 pts., and 60/135 also showed paratyphia, atypia, and hyperplasia, with malignant characteristics in at least 43/135; 7/135 (5%) underwent malignant transformation within 4-48 mo. of observation. In 5/68 pts. with chronic hypertrophic laryngitis planocellular carcinoma was also present; in 10/68, despite the initial clinical diagnosis of cancer, only precancerous changes were evident microscopically for several mo. before the malignant transformation occurred. Among 483 pts. who underwent excision of laryngeal polyps, 103/483 showed marked cornification, 12/483 acanthosis, hyperplasia, paratyphia and atypia and 3/483 showed a tendency for malignant degeneration. The clinical status of 2 pts. observed over a period of several yr. changed from hypertrophic laryngitis to acanthosis, and then to planocellular carcinoma. A man who developed hoarseness since beginning to work in a petroleum refinery and who worked for several decades with cresol, dichloro-octane and chromic acids, presented with a squamous cell carcinoma of the true vocal cords. Laryngeal cancer was also found in a woman who underwent irradiation for tuberculous lymph nodes

(neck) 18 yr. previously, and suffered chronic laryngeal inflammation since that time. Cancer of the larynx was found in 3/59 with laryngeal tuberculosis. Among 144 pts. with laryngeal papillomas, 11 pts. (7.6%) showed malignant transformation within several yr. of observation. Among 18 pts. with carcinomatoid papilloma, 4 developed squamous cell cancer within 2 mo.

- 64-1149 LEUKEMIA MORTALITY IN INFANCY. ITS ALLEGED DECLINE. (E.) Hewitt, D. (Dept. Social Med., Oxford U., England). New Eng. J. Med. 270(18):932-935, 1964.

From 1940-49 the infant death rate from leukemia per 1,000,000 live births in the U. S. was 41.8 among whites and 22.9 among non-whites and for 1950-59, 27.9 and 23.6, resp. For these 2 periods, these figures were 60% and 12% higher, resp., than those for infants in England and Wales. In Italy the mortality rate from leukemia at ages under 2 yr. is similar to that of U. S. whites, but for children age 3-4 the Italian rate is little more than half the American rate. The certified deaths from leukemia/1,000,000 white live births in 5 states (Alabama, Kentucky, Tennessee, Texas and West Virginia) with high anemia rates and 6 states (California, Illinois, Massachusetts, Nebraska, New York and Washington) with low anemia rates were 41.0 and 27.4 from 1950-54 and 27.5 and 25.9 from 1955-59, resp. The author reviews the possible explanations for this alleged decline: increase in av. duration of the disease, exclusive cause-of-death categories, greater accuracy in diagnosis, etc.

- 64-1150 MALIGNANT NEOPLASM MORTALITY IN THE COMMUNITY OF CATANZARO DURING THE FIFTY YEAR PERIOD FROM 1911-1960. (It.) Landolfi, L. (Inst. Anat., U. Naples, Italy). Boll. Fond. Pascale Tumori 8(1-2):33-44 and 50-56, 1961.

In a statistical survey of cancer mortality in the community of Catanzaro (Calabria) from 1911-1960, the av. cancer mortality indexes (per 100,000 inhabitants) were highest (71.72 and 68.1) for the 5-year periods 1951-1955 and 1956-1960, resp., and lowest (44.7 and 41.82) for 1936-1940 and 1931-1935, resp. When based on total deaths, the rate ranged from a minimum of 1.34% in 1912 to a max. of 11.28% in 1957-1958. Although earlier yr. indicated a higher incidence of mortality in females, the later yr. showed a reversal (male:female ratio of 38:25 for 1960) coinciding with the rise seen in national cancer mortality statistics for Italy. With regard to localization, a marked increase of frequency was noted in later yr. for cancer of the respiratory tract, stomach and liver, and leukemia, a moderate increase in genital cancer and a decrease in the frequency of malignant bone tumors. The most frequent neoplasm sites (in decreasing order) were stomach,

liver and lung in males and uterus, stomach, breast and liver in females. Identical frequencies (approx. 18.6%) were noted for neoplasms of the uterus and stomach when males and females were added together. A surprising increase in hepatic cancer was seen, consistent with recent findings, but the author feels that a large part is metastatic, and not primary. Age ranged from 3 mo. to 94 yr.; highest frequencies were between the ages of 40-80 yr. with a max. between 61-70 yr. In females with genital cancer, highest percentages were found in married women, but frequencies in widows and unmarried women were also high. As for occupation, highest incidence was seen among farmers and laborers in males and in housewives, but the figures were insignificant.

- 64-1151 CHRONIC ACTINIC CHEILITIS AND CANCER OF THE LOWER LIP. (E.) Nicolau, S. G. (Dermato-Venereol. Ctr., Bucharest, Rumania) and L. Băluș. *Brit. J. Derm.* 76(6):278-289, 1964.

Of 542 pts. with relatively well-defined lesions of actinic cheilitis (AC), 489 came from a fishing or agriculture settlement where they spent considerable time outdoors. In addition, 9 of these pts. showed other lesions of photosensitivity. From a second group of 76 pts. with epitheliomas of the lower lip, 47 displayed concomitant AC lesions: 44/76 were farmers, 11/76 were car drivers or construction workers. The 21 urban pts. of this group were free of AC lesions; leukoplakia, as a precancerous lesion, was recorded in 19/76 cases. The av. latent period between the appearance of AC lesions and development of epithelioma was 20-30 yr., but 1 pt. developed an epithelioma 3 yr. after the onset of AC. The incidence (47 total) in relation to the age at which epithelioma appeared was as follows: >70 yr. in 5; 60-70 yr. in 17; 50-60 yr. in 13; 40-50 yr. in 8; <40 yr. in 4. The microscopic pattern of AC is described in detail; this study also contributes evidence that chronic AC is a precancerous dermatosis.

- 64-1152 MORTALITY FROM MALIGNANT NEOPLASMS IN MOSCOW. (Rus.) Straus, Z. E. (1st Moscow Inst. Med. (Order Lenin), USSR). *Klin. Med. (Moskva)* 42(4):38-41, 1964.

Mortality/100,000 due to malignancies in 1958 in people aged 60 or more yr. (males--1241.0 (60-69); 1970.1 (70 or over); females--576.3 and 1159.5, resp.) was 10-15 times higher than in the age group 30-39 yr. (males 27.5; females, 31.8). Mortality was markedly increased for males age 15-19, 40-49, 50-59 and 60-69 (7.25, 156.8, 486.2, 1,241.0; females 1.16, 118.2, 283.1, 576.3, resp.). Mortality was higher in females of age 20-29 and 30-39 (6.48, 31.8; males 5.66 and 27.5, resp.). Mortality for the yr. 1937, 1947 and 1958 was, resp., for various cancers: stomach 47.4, 56.9 and 69.8; respiratory organs 10, 17 and 30.8; other digestive organs 11.1, 16.9 and

24.5; esophagus 12.1, 13.3 and 13.3; breast 2.6, 3.8 and 7.4; uterus 7.5, 10.1 and 9.6; female genital organs 1.2, 2.8 and 4.8; all malignant neoplasms 109, 135.3 and 177.1. Standardized indices of mortality (per 100,000) in Moscow for 1958 for males and females were, resp., 232.7 and 130.1. Highest mortality was in males from cancer of the esophagus, larynx and large intestine (98, 58.7 and 20.3, resp.); in females from cancer of the esophagus, large intestine and certain respiratory organs (47.9, 16.1 and 13.9, resp.).

- 64-1153 STATISTICAL STUDIES OF LEUKEMIA IN JAPAN. (Jap.) Wakisaka, Y. (Dept. Int. Med., Kyoto U. Sch. Med., Japan). *Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Japon.)* 26(1):107-109, 1963.

The total number of cases of leukemia reported from 123 hospitals in Japan during the period 1956-1961 was 2,676, of which acute myeloid leukemia (AML) represented 55.3%; acute lymphatic leukemia (ALL), 9.1%; acute unclassifiable leukemia, 6.5%; chronic myeloid leukemia (CML), 19.4%; chronic lymphatic leukemia (CLL), 2.4%; and monocytic leukemia, 7.3%. The acute form represented 70.9%, the chronic form 21.8%. In a total of 195 cases of ALL, the incidence was highest in the age group of 0-4 yr. (incidentally, higher than AML in this age group) and gradually dropped as age increased. In 161 cases of monocytic leukemia, the incidence was approx. identical in age groups from 0-4 yr. through 50-54. In 417 CML cases, the age incidence almost paralleled that of the entire group of chronic leukemia pts., with its peak in the age group 30-34 yr. In 54 cases of CLL, the highest peak was in age group 45-59 yr. Out of the total of 2,676 leukemic pts., 781 were less than 14 yr.; 1,077 were 15-39 yr.; 818 were more than 40 yr. There were no significant differences related to sex in any of the age groups.

- 64-1154 INCIDENCE OF ACUTE LEUKEMIA (MYELOID AND LYMPHATIC) IN CHILDREN IN JAPAN. (Jap.) Otani, T. (Dept. Pediat., Hiroshima U. Sch. Med., Japan). *Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Japon.)* 26(1):149-151, 1963.

On the basis of a statistical analysis of the incidence of leukemia of children reported from 10 Japanese university hospital pediatric departments (during the last 10 yr.), the author encountered a total of 401 cases. Of these 401, 385 (96%) were of the acute form and were classified as follows: myeloid, 247 (61.7%); lymphatic, 75 (18.7%); monocytic, 31 (7.7%); erythroleukemia, 5 (1.7%); and unclassifiable, 27 (6.7%). There were 14 chronic cases (10.0%), all myeloid. Age distribution was as follows: 214 (53.4%), 0-5 yr.; 127 (31.7%), 6-10 yr.; and 58 (14.5%), 11-14 yr. The male and female ratio was 1:0.71. Out of the 385 cases of the acute form, 237 were leukemic and 136, aleukemic; 1/14 cases of the chronic form was aleukemic.

- 64-1155 CYBERNETIC ASPECTS OF THE PREVENTIVE AND THERAPEUTIC MECHANISMS OF TWO SOCIAL DISEASES: CANCER AND RHEUMATIC DISEASE. (It.) Huant, H. (Radiobiol. Ctr., Paris). *Minerva Med.* 55(29):1100-1105, 1964.

In an evaluation of the applicability of cybernetic analysis to cancer and rheumatic disease, the author compares the source of informational error in both diseases. For cancer this source is intracellular and at an enzyme level; for rheumatic disease this source is extracellular and reflects concomitant electrolytic disturbances at the neurovascular level. In applying cybernetics to cancer probability, it is necessary to add mortality incidence to the number of living cases in the sociologic nucleus examined at a given chronologic interval of time. For cancer, the diencephalon-pituitary system and its effect on growth and anti-growth equilibrium is an important probability factor. The sociologic implications of cybernetics are also discussed.

- 64-1156 GALLBLADDER CARCINOMA IN CHOLELITHIASIS. A STUDY OF PROBABILITY. (E.) Newman, H. F. (Union Health Ctr., New York City) and J. D. Northup. *Geriatrics* 19(6):453-455, 1964.

In a statistical study on gallbladder carcinoma and cholelithiasis in Negroes and whites, the percentage of cases with gallbladder carcinoma (based on autopsy figures from 2,116 cases) and the calculated annual death rate (per 10,000) from gallbladder carcinoma in persons with stones for age groups 40-49, 50-59, 60-69 and 70-79 were found to be 13.9% and 3.07, 29.4% and 5.16, 33.7% and 5.68 and 16.5% and 4.17, resp.

- 64-1157 LEUKAEMIA IN AN AUSTRALIAN ABORIGINAL. (E.) Dougan, L. (Dept. Hemat., Royal Perth Hosp., Western Australia) and H. J. Woodliff. *Med. J. Aust.* 1(20):760-761, 1964.

A case history is presented of a 70-year-old Full-blooded Australian aboriginal woman with acute myeloblastic leukemia. Of 510 cases of leukemia and allied disorders recorded in a survey conducted in Western Australia, this is the only case reported in an aboriginal and is considered the first case on record.

- 64-1158 THE PROBLEM OF THE MALIGNANT CHANGE OF HEMORRHAGIC ULCERATIVE COLITIS. (Fr.) Draoui-Mahfoud, D. *Concours Med.* 6(12):1876, 1964.

The incidence of cancerous transformation appears to be 30 times greater in pts. with hemorrhagic ulcerative colitis than in the rest of the population. This incidence increases with the duration of the colitis and, after 10 yr., is as high as 20-30%. Sex does not appear to be a

determining factor; cancer usually appears between the ages of 25-50 yr. Pseudopolyposis seems to be an intermediate stage between hemorrhagic ulcerative colitis and the neoplasm, a mucous-secreting colloidal epithelioma. (See also CRA 1(3):#545, 1963.)

- 64-1159 LUNG CANCER AND SMOKING. (E.) Lees, T. W. (Law Hosp., Carlisle, Scotland). *Lancet* 1:1393-1394, 1964.

The statistical association between lung cancer and smoking can be simply explained: only previously healthy men (those who can indulge social habits, such as excessive smoking and drinking, and going to football matches) are certified as dying from acute disease. The chronically ill do not indulge in such habits to the same degree and are certified as dying of a chronic disease. Several studies indicate that the degree of association between smoking and any disease is related to the acuteness of death from that disease. Changes in the rate of a number of cancers are also cited; cancers come and go in successive overlapping waves, the wave of each type having a period of about 100 yr. Statistics are also cited indicating that lung cancer death rates at all ages under 55 have been declining over the past 5 yr.

- 64-1160 LUNG CANCER AND SMOKING. (E.) Editorial. *Lancet* 1:1374-1375, 1964.

In a leading article commentary on the previous paper, it is pointed out that the Royal College of Physicians, R. Doll and A. B. Hill, and the U. S. Surgeon General's Committee examined alternative theories and decided that the general theory was more plausible than any of those proposed. That chiefly the healthy individuals succumb to 'acute' diseases such as lung cancer is contrary to established facts since, for instance, smoking is known to be associated with chronic bronchitis and chronic bronchitis is itself associated with an increased liability to lung cancer. The 100-yr. cycle of cancers is questioned in view of lack of data as to site for such a period and if available would be questionable in terms of sustained accuracy of diagnosis over such a period. A more detailed analysis of pertinent mortality data is also provided.

- 64-1161 PROBLEMS ENCOUNTERED IN THE PATHOLOGY OF CHILDHOOD NEOPLASMS IN ARGENTINA. (Fr.) Besuschio, S. C. (Municipal Inst. Child. Surg., Buenos Aires, Argentina). *Ann. Chir. Infant.* 4(4):313-320, 1964.

A survey of tumor incidence among subjects between the ages of 0-15 yr. conducted in Argentina between 1960 and 1963 revealed a total of 262 tumors in 22,475 histologic examinations; 76/262, or 29%, were malignant. According to geographic distribution, highest frequencies were seen in the regions

of Buenos Aires, Santa Fe and Cordoba. Highest incidences (6-7 cases each) were seen for ages 3-5, 10, and 13-15 yr. The most frequently involved sites were: lymph glands, 24 cases; bone, 10; kidney, 8; soft tissue, 8; eye, 8; retroperitoneum, 4; ovary 4. According to tumor type, the female incidence, male incidence and av. age in yr. was as follows: 6, 10 and 8, resp., for malignant lymphoma and leukemia; 1, 7 and 8 for Hodgkin's disease; 4, 3 and 4 for embryonal symphoma; 4, 3 and 2.5 for Wilms's tumor; 3, 2 and 8.5 for Ewing's tumor; 5, -- and 10 for malignant ovarian tumor; 1, 3 and 8 for reticulum cell sarcoma; 3, -- and 2 for retinoblastoma; --, 3 and 6 for glioma; --, 3 and 8 for malignant tumor of the testicle.

- 64-1162 CARCINOMA AND ANTHRACOSILICOSIS. (E.) Nealon, T. F., Jr. (1012 Walnut St., Philadelphia, Pa.). *Arch. Environ. Health* 8(6): 882-885, 1964.

In a clinical discussion of anthrasilicosis, analysis of 1,000 consecutive cases of lung carcinoma observed at Jefferson Medical College revealed that 118 came from the Pennsylvania anthracite counties. All of the 109 men were not miners, but all had been exposed to coal dust.

- 64-1163 BULLETIN OF BIOSTATISTICS AND EPIDEMIOLOGY. NO. 10. (BOLETIM DE BIOESTATISTICA E EPIDEMIOLOGIA NO. 10). Fund. Servico Espec. De Saude Publ. Div. Orient. Tecnica. Rio de Janeiro, Brazil, 128 pp., 1960.

Morbidity and mortality data for infants and adults in the various states of Brazil, including data on deaths due to neoplasms per 100,000 population in the yr. 1959 and 1960 are presented.

- 64-1164 LUNG-CANCER MORTALITY AS RELATED TO RESIDENCE AND SMOKING HISTORIES. II. WHITE FEMALES. (E.) Haenszel, W. (NCI, Bethesda) and K. E. Taeuber. *J. Nat. Cancer Inst.* 32(4): 803-838, 1964.

When residence and smoking histories along with other necessary diagnostic details were collected for a 10% sample of all white female lung cancer deaths in the U. S. during 1958 and 1959 and compared with a sample of the general population many findings agreed with those reported earlier for males: higher lung cancer risk associated with the number of cigarettes smoked, urban residence, with mobile populations with 3 or more exposure residences and for foreign-born; farm-born migrating to urban counties constituted a special high risk group. The major difference between results for each sex is that female smokers residing in urbanized areas did not display risks higher than those expected from the sum of 2 separate smoking and residence effects. Among nonsmokers, the male:female ratio for lung cancer

deaths was about that for other causes of death (1:3). Male smokers of 1 pack or less and more than 1 pack of cigarettes daily had lung cancer rates 4 times higher than for corresponding females.

- 64-1165 PROBLEMS AND RESULTS OF A CLINICAL-STATISTICAL STUDY OF LARYNGEAL CARCINOMA. (Ger.) Fendel, K. (Ear-Nose-Throat Clin., U. Jena, Germany), H. Teichert and G. Funk. *Wiss. Zschr. Friedrich-Schiller Univ. Jena/Thür. (Math. Naturwiss.)* 12(2/3):205-235, 1963.

After a discussion on the problems of standardizing cancer statistics (including statistical units of measurements and methods of calculation), the authors present 588 cases of laryngeal carcinoma collected during 1932-1955 from the Jena's Otorhinolaryngological Clinic with respect to the duration of symptoms, main symptoms, localization, stages, age and treatment. The area served by the clinic was at times neither uniform nor sharply limited and so it is not possible to decide, from the number of clinically known cases, about the incidence of carcinoma in the population.

- 64-1166 MALIGNANT TUMORS IN ELDERLY PATIENTS. (It.) Iapichino, A. (Dept. Public Health, Rome) and D. Sanguigni. *Riv. Geront. Geriat.* 12(3):89-96, 1963.

In a survey conducted by a national health insurance group throughout Italy, the following age distribution was reported for 1,706 pts. with malignant tumors for a 1-yr. period from October, 1961 to October, 1962: 45-49 yr. 11%; 50-54 yr. 20%; 55-59 yr. 18%; 60-64 yr. 13%; 65-69 yr. approx. 18%; 70 yr. and over 20%. In the 1,507 pts. over 45 yr. old the male/female ratio was 607:900; the male/female ratio for cancer risk was 343,659:322,032 and 388,819:363,792 for 1961 and 1962, resp. Highest incidence of malignancy (in decreasing order of frequency) was found in the following regions: Emilia, Venice, Latium-Umbria, Tuscany, Sicily, Piedmont, Lombardy, Liguria, Apulia, Marches and Campania. According to systems involved, the male/female sex distribution and age group with the highest incidence was as follows: 215/202 and 70 yr. or over for digestive tract; 157/32 and 50-54 yr. for respiratory tract; 517/63 and 50-54 yr. for genital tract; 45/13 and 50-54 yr. for urinary tract; 76/80 and 70 yr. and over for nervous system, skin, connective tissue; 39/30 and 55-59 yr. for blood and lymph system; 12/26 and 70 yr. or over for unspecified systems. The most frequent anatomic site was the female genital tract with 517 cases, of which 301 breast and 181 uterus, and with highest incidence between the ages of 50-60 yr.

- 64-1167 CHRONIC ULCERATIVE COLITIS AND CARCINOMA OF THE COLON. (E., Abstract) Farmer, R. G. (Cleveland Clinic, Cleveland, Ohio),

R. J. Diaz and C. H. Brown. Gastroenterology 46(6):741, 1964.

Among 1,258 pts. with chronic ulcerative colitis seen at the Cleveland Clinic from 1950-1963, 23 (1.8%) had carcinoma of the colon. Mean age of onset of colitis was 22.6 yr.; the mean age of diagnosis of carcinoma was 40.7 (16-67 yr.). Multiple carcinomas (including 7 with multifocal carcinoma *in situ*) were found in 12/23. Carcinoma of the colon occurs at an earlier age and is more highly malignant when associated with ulcerative colitis than when alone.

64-1168 11. LARYNGEAL CARCINOMA IN WOMEN. (Ger.) Fendel, K. (Ear-Nose-Throat Clin., U. Jena, Germany), H. Teichert and G. Funk. Wiss. Zschr. Friedrich-Schiller Univ. Jena/Thür. (Math. Naturwiss.) 12(2/3):237-258, 1963.

Among a total of 588 pts. with laryngeal carcinoma (see CRA 2(6):#1165, 1964) only 51 were women. The av. age of the female pts. was 4.2 yr. lower than in men (i.e., 55.3 yr. and 59.5 yr., resp.), a statistically significant difference. The av. age of women with cancer of the glottic region and tumors of all regions was 7.8 and 4.8 yr. lower than that of men.

64-1169 FURTHER EVALUATIONS OF THE GEOGRAPHICAL DISTRIBUTION OF LEUKEMIA IN THE CRACOW REGION. (Pol.) Janicki, K. (3rd Clin. Int. Dis., Acad. Med., Cracow). Pol. Arch. Med. Wewnet. 34(6):699-702, 1964.

The statistically evaluated incidence of all types of leukemias in the Cracow region during 1951-1960 was found not to be correlated with the density of population or geographic distribution. See also CRA 2(2):#374; and *ibid.*, (3):#548, 1964.

64-1170 EVALUATION OF CLINICAL MALIGNANCY OF CANCER OF THE ORAL CAVITY. (Pol.) Pawlicki, M. (Inst. Oncol., Cracow) and A. Chrzanowski. Nowotwory 14(2):93-96, 1964.

During 1951-1962 the authors treated 1435 men and 123 women with the following cancer: 1415, lip; 62, tongue; 81, oral mucosa. Average ages in the 3 groups were 57.1, 60 and 55 yr., resp. Farmers constituted 60%, 38.7%, and 32%, resp.; manual workers made up 35%, 30.6%, and 37%, resp.; metastases to cervical lymph nodes were found in 7.6%, 38.4%, and 71.4%, resp.

64-1171 FAMILIAL PHEOCHROMOCYTOMA AND THYROID CARCINOMA. (E.) Nourak, D. S. (3333 E St., San Bernardino, Cal.). Ann. Int. Med. 60(6):1028-1040, 1964.

The association of familial bilateral pheochromocytoma and thyroid carcinoma in a mother and daughter is reported. A familial occurrence of pheochromocytoma has been reported previously in 17 kindreds. The pheochromocytoma was multiple in 25/54 (46%) familial cases, but only in 10% of sporadic cases. Among the associations noted were with multiple neurofibromatosis, Von Hippel-Landau's disease, sarcoma and thyroid carcinoma.

64-1172 CLINICAL AND STATISTICAL STUDIES OF TUMORS OF RETICULOENDOTHELIAL SYSTEM IN JAPAN. (E.) Kimura, K. (Dept. Int. Med., Natl. Cancer Ctr. Hosp., Tokyo, Japan). Tohoku J. Exp. Med. 82(1):1-20, 1964.

Statistical studies conducted among 1,443 pts. with tumors of the RES treated from 1953-63 at various hospitals in Japan revealed the following distribution: reticulum cell sarcoma of lymphoid tissue 1169 cases (81.0%), reticulum cell sarcoma of various organs 130 (9.0%), Ewing's sarcoma 58 (4.0%), reticuloendothelioma 54 (3.7%) and reticulum cell sarcoma of bone 32 (2.2%). A survey conducted among 2,188 pts. with lymphoid tissue tumors for the same period showed the following distribution: reticulum cell sarcoma of lymphoid tissue 1,169 cases (53.4%), Hodgkin's disease 459 (21.0%), lymphosarcoma 313 (14.3%), lymphatic leukemia 156 (7.1%), follicular lymphoblastoma 38 (1.7%) and unclassified malignant lymphoma 53 (2.4%). In both of these large series, disease was more frequent in males. Highest incidence of reticulum cell sarcoma was seen in the age group 55-65, of reticulum cell sarcoma of bone in age groups 20-30 and 55-60, and Ewing's sarcoma in pts. <25. A significant difference in age distribution was observed between Japan and other countries. The incidence of reticulum cell sarcoma and leukemia in pts. >55 yr. old is increasing in Japan. Past association with tuberculosis and syphilis was infrequent. An extensive report of clinical and hematologic findings, physiopathology and effects of therapy in pts. with tumors of RES and lymphoid tissue is also presented. (See also the following abstract.)

64-1173 PATHOLOGICAL STUDIES OF TUMORS OF RES IN JAPAN. (E.) Akazaki, K. (Dept. Path., Tohoku U. Sch. Med., Sendai, Japan) and H. Wakasa. Tohoku J. Exp. Med. 82(1):21-41, 1964.

In a statistical survey conducted from 1955-61 at the Pathology Department of the University of Tohoku, tumors of the RES were found to constitute 184/24,292 (0.75%) biopsies and 41 (40)/1,465 (2.8%) autopsies, as well as 5.4% of the total malignant tumors observed in this period. According to RES tumor type, incidence from autopsy and biopsy was, resp., as follows: 26/41 (63.4%) and 139/184 (75.9%) for reticulum cell sarcoma (r.s.); 5/41 (12.1%) and 24/184 (13.1%) for Hodgkin's disease (h.d.); 4/41 and 0/184 for reticuloendothelioma of the liver; 3/41 and 9/184 for Ewing's

tumor; 1/41 and 0/184 for Lindau's tumor; 2/41 and 0/184 for leukemic reticuloendotheliosis; 0/41 and 12/184 for other tumor types. R.s. incidence showed a peak (approx. 24% of cases) between the ages 40-50, while no significant age characteristics were observed for h.d. The incidence of r.s. and h.d. was 68.3% and 19.6%, resp., for all of Japan, but lower r.s. incidence (28.5%) and higher h.d. incidence (71.5%) were observed in the combined autopsies and biopsies of other foreign countries. Upon classification of r.s. according to site of growth, the lymphatic type showed the highest incidence. (See the preceding abstract.)

- 64-1174 LEUCOPLAKIA BUCCALIS. (E.) Cooke, B. E. D. (Dept. Oral Med., U. Wales, Cardiff). *Ann. Roy. Coll. Surg. Eng.* 34(6): 370-383, 1964.

The author reports on 50 cases (41 male, 9 female; age 20-60 yr.) of leukoplakia observed personally from 1952-61; 12% underwent carcinomatous change. In 6 pts. the leukoplakia proved to be a carcinoma at the first biopsy, or subsequently developed into one. Dyskeratosis was seen in 20/50 pts. and 30% of these 20 were malignant or soon became so. In the remaining cases, keratosis or parakeratosis with or without acanthosis was usually observed. The author advocates the classification of leukoplakia into dyskeratotic and non-dyskeratotic forms. Friction alone or in combination with smoking or betel nut chewing is an all-important factor.

- 64-1175 FEMALE GENITAL CARCINOMA AND THYROID DISEASE. (E.) Berggren, O. G. A. (Dept. Gynec., Radiumhemmet, Stockholm, Sweden). *Acta Obstet Gynec. Scand.* 42(4):425-437, 1964.

In 187 pts. with ovarian carcinoma observed from 1946-1962 at Linköping and Norrköping as well as 5819 pts. with cervical carcinoma seen over 1946-1960 at Radiumhemmet, the incidence of thyroid disorders was 11.23% and 3.27%, resp. In 4935 controls, incidence of thyroid disorders was 2.94%. The results support the supposition of a connection between carcinoma and thyroid disease and indicate that the frequency of thyroid disorders increases more in the ovarian than in the cervical carcinoma pt.

- 64-1176 MALIGNANT PULMONARY TUMORS IN TUBERCULOSIS PATIENTS. (Heb.) Eitelson, P. (Centl. Clin. Zamenhof Health Insur. Fund, Tel-Aviv, Israel). *Harefuah* 66(10):344-347, 1964.

Three cases are reported in which lung carcinoma was associated with pulmonary tuberculosis. Onset was first detected radiographically but was proven clinically 10 mo. to 3 yr. later (2 at necropsy). This association may be expected to increase due to the greater frequency of pulmonary tuberculosis in older pts., especially men.

- 64-1177 ASBESTOS EXPOSURE AND NEOPLASIA. (E.) Selikoff, I. J. (Dept. Med., Mt. Sinai Hosp., New York), J. Churg and E. C. Hammond. *J.A.M.A.* 188(1):22-26, 1964.

In 632 male Caucasian insulation workers with a relatively light, intermittent exposure to asbestos for a period of 20 yr. or more (studied from Jan. 1, 1943 through 1962), the total number of deaths was 255, while the expected number was 203.5. As for causes of death, the actual number as compared to the expected number (in parenthesis) was as follows: cancer at all sites, 95 (36.5); cancer of lung and pleura, 45 (6.6); cancer of stomach, colon, rectum, 29 (9.4); cancer of all other sites combined, 21 (20.5); asbestosis, 12 (in pts. exposed from 32-59 yr.). Four mesotheliomas found (1 peritoneal and 3 pleural) represent an unexpectedly high incidence in 255 deaths. In 2 cases of diffuse pleural mesothelioma, asbestos bodies were observed. While smoking habits of the deceased were not given, it was estimated that smoking could not account for a lung-cancer mortality rate 6.8 times that of a random sample of Caucasian males.

- 64-1178 THE CLINICAL OBSERVATION OF MALIGNANT LYMPHOMA. A REPORT OF 27 CASES. (E.) Lee, S. Y. (Dept. Int. Med., Yonsei U. Coll. Med., Seoul, Korea) and Chai, E. S. *Korean J. Int. Med.* 7(5):281-288, 1964.

Data from a series of 27 pts. with malignant lymphomas (lymphosarcomas, 55.6%; reticulum cell sarcoma, 18.5%; Hodgkin's disease, 18.5%; follicular lymphoma, 7.4%) who were observed for 4 yr. and 9 mo. are presented. The ratio of male:female pts. was 2:1. Some cases were found in all age groups through age 60-69. Seven cases in males (none in females) occurred below age 29; highest incidence in females was age 30-39, highest for males, 40-49.

- 64-1179 BRONCHOGENIC CARCINOMA IN WOMEN. (E.) Hanbury, W. J. (Dept. Path., St. Bartholomew's Hosp., London, E.C.1). *Thorax* 19(4):338-342, 1964.

In 100 consecutive cases of women with pulmonary carcinoma, material of which was studied in the pathology department (av. age at diagnosis 58; range 12-75 yr.; 69/100 55 yr. old or more), smoking habits were as follows: 14 heavy smokers (at least 20 cigarettes daily); 24 moderate (at least 10 daily); 10 light (less than 10 daily); 3 very occasionally; 29 nonsmokers; 3 had smoked previously; 17 not classifiable. Carcinomas were classified as oat-cell (39), undifferentiated (23), squamous-cell (21) or adenocarcinoma (17). Undifferentiated tumors occurred more frequently in pts. <55 yr. old; oat-cell and squamous tumors were more frequent in the heavy-moderate smoker groups than in the remaining pts. In the 43 cases that came to necropsy, the most frequent metastatic sites (in decreasing order) were as follows:

hilar or mediastinal lymph nodes, liver, skeleton, abdominal lymph nodes, adrenal glands, cervical lymph nodes, pleura, lung, pericardium and brain.

- 64-1180 CONCORDANT DISEASE IN IDENTICAL TWINS. (E.) Heizer, W. D. (Dept. Med., Johns Hopkins Hosp., Baltimore, Md.) and E. F. Lewison. J.A.M.A. 188(3):217-220, 1964.

Two case histories are presented of 2 Negro twin (probably monozygotic) sisters with concordant breast cancer, diabetes mellitus, nontoxic goiter, hypertension, cholecystitis, obesity, relaxed pelvic outlet and uterine myomas. A brief review of literature (18 references) describing mammary cancer in identical twins is also presented.

- 64-1181 GASTRIC STUMP CARCINOMA FOLLOWING RESECTION FOR PEPTIC ULCER. (Ger.) Enderlin, F. (Dept. Surg., U. Basel, Switzerland). Med. Hyg. (Geneve) 22(647):583-584, 1964.

Between 1952 and 1964, 12 gastric stump carcinomas after stomach resection for peptic ulcer were observed at the University of Basel. The av. age of the pts. at the time of resection was 39 yr. and av. interval between resection and development of carcinoma was 22 yr. Only 4/12 were diagnosed correctly at the first consultation and hence, 8 were found inoperable.

- 64-1182 PROBLEMS, TASKS AND LIMITS OF PSYCHOSOMATIC CANCER RESEARCH. (Ger.) Baltrusch, H.-J. F. (19 Babenend St., Oldenburg (Oldb.), Germany). Zschr. Psychosom. Med. 9(4):285-294, 1963.

The problems and tasks confronting psychosomatic cancer research are seen to fall into five major categories including (1) psychological studies; (2) psychophysiological investigations in cancer pts.; and (3) psychosomatic animal experiments. Under (1), some specific problems mentioned are: effect of personality patterns on the development of the disease and its progress; definition of a "cancer prone personality"; affinity of certain types of malignancies to different psychodynamic personality types; evaluation of psychological states such as despair, depression, etc., as contributing factors; incidence of cancer in persons with abnormal or psychotic behavior patterns (criminals, prostitutes, mental pts., etc.); group investigations

on a transcultural basis in various countries, civilizations, races and societies; investigation of the everyday habits of cancer pts., especially with regard to eating, smoking, and drinking habits; and comparison of different age groups characterized by a high incidence of cancer, such as childhood and old age. Under (2), the author lists studies on nervous functions, hormonal balance, immunological reactions; the role of chronic inflammations and trauma; and analysis of the previous history of the cancer pt. with respect to psychosomatic background data. Under (3), it is advocated that psychosomatic animal experiments be conducted in species "sociologically close" to man, such as the domestic dog.

- 64-1183 PRIMARY CARCINOMA OF THE GALLBLADDER: (A NOTE ON TWO CLINICAL CASES.) (Por.) Raposo, L. J. (U. Coimbra Sch. Med., Portugal). J. Med. (Porto) 64:388-394, 1964.

Two female pts. (age 53 and 62 yr.) are presented who were found to have adenocarcinoma of the gallbladder associated with cholelithiasis. The author stresses that the chronic irritation of calculi may be a factor in the development of gallbladder carcinoma.

- 64-1184 SEVERE ULCERATIVE COLITIS AND CANCER. (Sp.) Ramos Mejia, M. M. Prensa Med. Argent. 50(40):2605-2606, 1963.

Among 97 cases of severe ulcerative colitis who were hospitalized at an institution in Argentina between 1951 and 1959, 4 (4.1%) were found to have an adenocarcinoma of the colon. Interval between onset of colitis and diagnosis of cancer ranged from 12 to 27 yr. (av. 20 yr.); age at the time of cancer diagnosis was 24-42 yr. Among 6321 pts. with various gastrointestinal disorders seen during the same period, 522 were reported to have a carcinoma of the rectum and colon.

- 64-1185 KRAUROSIS VULVAE AND GASTRIC CANCER. (Hun.) Szendi, B. Magy. Onkol. 1(8):53-57, 1964.

Three cases are presented and discussed of kraurosis vulvae with simultaneous gastric cancer. This association was not seen in 15 pts. admitted subsequently with kraurosis vulvae. Of the 177 pts. with kraurosis seen over the past 12 yr., 22 (13.3%) also had cancer of the pubic regions.

See also abstract nos.: 1027, 1058, 1110

MISCELLANEOUS

64-1186 HISTOCHEMICAL STUDY OF THE PERIPHERAL NERVOUS SYSTEM IN UTERINE CANCER.

(Jap.) Hashimoto, M. (Dept. Obstet. Gynec., Tōhoku U. Sch. Med., Japan). Nippon Sanka Fujinka Gakkai Zasshi (J. Jap. Obstet. Gynec. Soc.) 15(10):938-946, 1963.

Histological study of peripheral nervous system of uterine cervical tissue was studied in 20 pts. with uterine carcinoma by the Seto silver plating method, a modification of the Bielschowsky staining method. Vegetative nerve endings which were usually demonstrated in normal cervical tissue were not found in cases with carcinoma, even in extremely early stages; instead, various kinds of degenerated nerve fibers were seen. No regenerated nerve fibers were found. The relationship between the nervous system and carcinogenesis on the growth of uterine cervical carcinoma was discussed along with a review of the literature (45 references).

64-1187 A CASE OF LIP CANCER DEVELOPING AFTER CHRONIC DISCOID LUPUS ERYTHEMATOSUS.

(Jap.) Kobayashi, T. (Dept. Dermatol., Chiba U. Sch. Med., Japan). Hifuka No Rinsho (Clin. Derm., Tokyo) 5(12):837-841, 1963.

A 41-year-old Oriental male with a 10-year history of chronic lupus erythematosus of the face, developed a spindle cell carcinoma of the lower lip, 10 mo. after admin. of atabrin, bismuth nitrite and quinine chloride for 2 mo. All cases of lip cancer developing after lupus erythematosus (14) and lupus vulgaris (19) in Japan are reviewed (6 references).

64-1188 PROLIFERATIVE DISORDERS OF THE BONE MARROW. (Sp.) Altafulla, M. Arch. Med. Panamen. 12(2):149-159, 1963.

The incidence, characteristic laboratory findings, presenting symptoms and prognosis of 5 related bone marrow disorders are reviewed in detail: myeloid metaplasia of unknown origin (most frequently in persons over 40); polycythemia rubra vera (highest frequencies between ages 40-60 and among males); a preleukemic syndrome consisting of leukocytosis, massive proliferation of thrombocytes, venous thrombosing and hemorrhage (seen most frequently in pts. in their 30's); Di Guglielmo's syndrome; and chronic myeloid leukemia. The author concludes that all 5 represent variations of a single, pathological reaction pattern following stimulation by an unknown agent of the reticuloendothelial tissue in different stages of development. He cites in support of this conclusion the fact that a gradual transition from one syndrome to the other has been reported in pts. under chemotherapeutic management.

64-1189 COMPARATIVE STUDIES ON LYMPHOBLASTIC LEUKEMIA IN AXENIC AND CONVENTIONAL MICE. (E., Abstract) Nielsen, A. H. (Dept. Microbiol., U. Kansas Sch. Med., Kansas City) and A. A. Werder. Fed. Proc. 23(2)(Pt. 1):392, 1964.

In 200 uninoculated conventional CFW mice, the incidence of death from leukemia over a period of 24 mo. was 23% in males and 29% in females, with median age of death of 8 and 9 mo., resp. On the other hand, conventional mice inoc. with non-leukemic liver extracts showed an incidence of 28% for males and 34% for females. No deaths from leukemia occurred in 165 uninoculated axenic CFW mice in a 12-mo. period, or in 39 inoc. axenic mice over the same period. Inoculation of leukemic tissue into axenic mice did result in leukemia, but at a lower rate (after 6 mo.) than in conventional mice. Ex-axenic mice showed low incidence (4%) of leukemia in 12 mo., but if they were foster-nursed on conventional mice previously inoc. with leukemic tissue, the incidence was 67% within 6 mo.

64-1190 EFFECT OF PROTEOLYSIS BY PAPAIN ON METASTASIBILITY OF TUMOR CELLS FROM THEIR PRIMARY GROWTH INTO BLOOD AND ORGANS OF THE MOUSE. (E., Abstract) Goldie, H. (Dept. Oncol., Meharry Coll. Med., Nashville, Tenn.), M. Walker, R. Flow and C. Walker. Fed. Proc. 23(2)(Pt. 1):287, 1964.

S-180 cells, after incub. in 1% or 1.5% papain soln. for 3-5 days, were inj. s.c. into 60 mice; similar inj. of cells incub. in saline were also made into 60 controls. After 5-6 days, when heart blood and liver brei were assayed for the presence of viable tumor cells, 7-12% of blood grafts and 3-8% of liver grafts in controls showed positive results compared to 2-6% and 0-3%, resp., in grafts of treated mice.

64-1191 MORPHOLOGICAL CHANGES IN MAMMARY GLAND CANCER OF RATS (RMK-1) UNDER CONDITIONS OF REPEATED TRANSPLANTS. (E.) Konoplev, V. P. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow) and N. D. Lagova. Bull. Exp. Biol. Med. 55(4):442-444, 1964.

This transplantable rat alveolar milk duct carcinoma (RMK-1), first obtained in 1958, has been carried through 32 generations, during which time it has undergone changes in both hormone reactivity and in structure. The tumor has become less differentiated as manifested by decreased secretion and decreased capacity to glandular structure formation. Some cytological dedifferentiation has also occurred as seen in the enlargement of the nucleus, a more distinct chromatin network, and separation of the nucleolus. There also have appeared areas of solid epithelial

growth and strata of atypical fibroblast-like epithelium. Mitoses have also increased, indicating an increase in tumor malignancy.

64-1192 MULTIPOTENTIALITY OF SINGLE EMBRYONAL CARCINOMA CELLS. (E., Abstract)

Kleinsmith, L. J. (Dept. Path., U. Michigan, Ann Arbor). *Fed. Proc.* 23(2)(Pt. 1):288, 1964.

From over 1500 single cells of an embryonal carcinoma grafted into mice, 44 clonal lines were obtained; 43 were teratocarcinomas composed of as many as 14 well-differentiated benign tissues plus embryonal carcinoma. These 43 lines showed marked degrees of differentiation, embryoid body production, and growth rate. The other clone showed limited potential for differentiation, producing only yolk sac, trophoblast and embryonal carcinoma. The findings were interpreted as giving strong support to the stem cell theory of cancer; they support neither the dogma of the irreversibility of malignant transformation or the somatic cell mutation theory.

64-1193 CARCINOMA OF THE TONGUE IN IDENTICAL TWINS. (E.) Covington, E. E. (Dept. Oncol., U. Maryland Sch. Med., Baltimore, Md.) and A. A. Bulls. *Am. J. Roentgen.* 92(1):213-214, 1964.

The occurrence of squamous cell carcinoma of the tongue (but each on a different side) is reported in monozygotic, Negro twins, age 46, who entered the hospital during the same mo. A review (3 references) of similar cases is presented which emphasizes the operation of an hereditary factor.

64-1194 POLYCYTHEMIA AND MYELOSCLEROSIS. (It.) Oliva, G. (Dept. Semeiol., U. Perugia, Italy), G. Silvestri and F. Pugliese. *Minerva Med.* 54(101):3885-3891, 1963.

The case history is presented of a 56-year-old woman showing an association of polycythemia vera and myelosclerosis. The author cites incidence of the above combination (25% of 250 cases) as reported by W. Dameshek; E. Chievitz and T. Thiede report a 19% incidence, more frequent in polycythemia pts. treated with X-rays; both R. Klima and W. Achenbach report an incidence of about 20%.

64-1195 STUDY OF KIDNEY SIZE IN POLYCYTHEMIA VERA. (E.) Hornung, N. (Roswell Park Mem. Inst., Buffalo, N. Y.) and L. Stutzman. *New York J. Med.* 64(7):882-886, 1964.

Of 24 pts. (age range 40-78 yr.; 12 males, 12 females) with polycythemia vera observed from December 1927 to March 1960 at the Roswell Park Memorial Institute, 13 (6 male, 7 female) had X-ray films from which kidney size could be

determined. Total kidney area enlargement was seen in 4/13 (31%) pts. These results did not support the hypothesis that hypertrophy of the kidney with resulting oversecretion of erythropoietin is of etiologic significance in polycythemia vera.

64-1196 REFRACTORY PRENEOPLASTIC SIDEROBLASTIC ANEMIA. (Sp.) Farreras Valenti, P. (Sch. Hemat., U. Barcelona, Spain), C. Rozman and S. Woessner. *Rev. Clin. Esp.* 92(1):12-16, 1964.

The authors present case histories of 4 pts. (2 male, 2 female; age 49-59 yr.) with idiopathic sideroblastic anemia which developed into malignant disease after a period of 18 mo. in 3 pts. and 5 yr. in 1 pt. The malignancies included: adenocarcinoma of the cecum 1; malignant abdominal tumor of undetermined origin and with brain metastases 1; myeloblastic leukemia 1; osteomyeloreticulosis 1. The authors emphasize the pre-cancerous significance of a refractory sideroblastic anemia appearing in adults between the ages of 45 and 60 yr. without apparent cause.

64-1197 KARYOTYPE STUDY OF MONOLAYER CULTURE OF HUMAN STOMACH CANCER CELLS. (E.)

Ugryumov, E. P. (Dept. Immunobiol., Inst. Exptl. Biol., Acad. Med. Sci. USSR, Moscow) and M. T. Tsoneva-Maneva. *Fed. Proc.* 23(3)(Pt. 2):T465-T467, 1964.

Cytogenetic examination of the 65th passage of Cave strain human stomach cancer cells revealed a relative uniformity with the number of chromosomes fluctuating between 58 and 62 in 81% of 100 cells examined; there were marked peaks at 58 and 60. Idiograms of single cells with 58, 60 and 62 chromosomes showed the long subtelocentric marker chromosome which is found in most cells of this strain. An additional large acrocentric marker chromosome was seen in the cell with 59 chromosomes. Other unpaired chromosomes were seen; the idiogram with 60 chromosomes showed small chromosome fragments. No annular chromosomes were noted.

64-1198 THE *IN VITRO* ACTION OF PHYTOHEMAGGLUTININ ON LYMPHOCYTES IN CHRONIC LYMPHOID LEUKEMIA. (Fr.) Bernard, C. (Inst. Leukemic Res., Saint-Louis Hosp., Paris), A. Gerales and M. Boiron. *Nouv. Rev. Franc. Hemat.* 4(1):69-76, 1964.

Comparative studies of the *in vitro* effect of phytohemagglutinin (P; 1 μ l of aqueous soln. per ml of cellular suspension) on lymphocytes taken from 13 normal subjects and 15 pts. (7/15 previously treated with chlorambucil) with chronic lymphatic leukemia reveal the presence of large nucleolated basophils showing mitotic activity. Leukemic lymphocytes showed the following: lower percentage of transformed cells, longer period to reach a max. of transformed cells and fewer

mitoses. No mitoses or cellular transformation were noted in specimens not treated with P.

- 64-1199 RECURRENT RETINOBLASTOMA IN ADULTHOOD. (Ger.) Lasch, H. (Eye Clin., U. Greifswald, Germany). *Klin. Mbl. Augenheilk.* 144(2):268-273, 1964.

A 40-year-old woman with a diagnosis of spontaneously healed retinoblastoma had to undergo unilateral enucleation 2 yr. later due to progressive retinoblastoma. Her 2 older children with retinoblastoma had to undergo bilateral enucleation by age 5.5 and 6.5 yr. and were alive at time of report. The youngest child died at the age of 3 yr. of advanced retinoblastoma. The dominant mode of inheritance is emphasized by the fact that each child had a different father. A fourth pregnancy was aborted for eugenic reasons. It was concluded that people affected with or cured of retinoblastoma ought not to have children.

- 64-1200 HEIGHTENED SUSCEPTIBILITY TOWARD CHEEK POUCH HETEROGRAFTS OF A MOUSE LEUKEMIA WITH SMALL DOSES OF LYOPHILIZED TISSUE. (E., Abstract) Adams, R. A. (Dept. Path., Harvard Sch. Med., Boston, Mass.). *Fed. Proc.* 23(2) (Pt. 1):238, 1964.

Previous experiments which indicated that heightened susceptibility to mouse leukemic heterografts in the Syrian hamster cheek pouch can be induced by prior immunologic sensitization of cortisone-conditioned hosts suggested that susceptibility might be related to a restriction of the quantity of antibody reaching the graft site, possibly resulting in inactivation of graft antigen without cytotoxic effects. Since theoretically the same results should be attained through minimal antigenic stimulation of the host, varying quantities of lyophilized leukemic cells were used for pretreatment and the amount needed to give the same degree of heightened susceptibility was reduced from totals of 180 mg to 2.5 mg.

- 64-1201 POLYPOIDY IN ACUTE CHILDHOOD LEUKEMIA. (E.) Davis-Lawas, D. (U. Philippines Coll. Med., Quezon City) and I. Lawas. *Acta Med. Philipp.* 19(3):43-49, 1963.

A case of acute stem cell leukemia is presented in an 8-year-old girl in which direct bone marrow examination revealed that 30% of the cells counted after anti-leukemic treatment showed an abnormal chromosome number: 11% were either hypo- or hyperdiploids and 16% were hypo-octaploids. The presence of polyploidy at the octaploid level with a skewed distribution of the chromosome counts is fairly uncommon in childhood leukemia. A brief review (17 references) of the rare cases found in the literature and a discussion of the possible causes of octaploidy are included.

- 64-1202 A MICROSOMAL DIFFERENCE BETWEEN NORMAL LIVER AND "MINIMAL-DEVIATION" HEPATOMA 5123 DETECTABLE BY ELECTRON SPIN RESONANCE. (E.) Nebert, D. W. (Dept. Biochem., U. Oregon Sch. Med., Portland) and H. S. Mason. *Biochim. Biophys. Acta* 86(2):415-417, 1964.

In 7 female Buffalo strain rats inoc. i.m. and s.c. with Morris hepatoma 5123-B with sacrifice 8 wk. later, the properties of various microsomal liver and hepatoma fractions were studied by electron spin resonance spectroscopy. The microsomal Fex content of the hepatoma was <33.3% that of the microsomes from healthy rat liver; a decrease was also noted in host liver. The Mn content of the hepatoma was two-fifths that of normal and host liver. The free radical content and the acetanilide-hydroxylase activity of the three groups of microsomes were not significantly altered.

- 64-1203 ANTI-M IN NEOPLASTIC DISEASE. (E.) Dunsford, I. (Nat'l. Blood Transf. Serv., Sheffield, England). *Vox Sang.* 9(2):212-213, 1964.

The isoantibody anti-M was not found in the sera of 506 pts. with known neoplastic diseases (66 reticuloses, 69 carcinoma of lung and bronchus, 59 carcinoma female reproductive organs, 93 squamous epithelium, 65 carcinoma of the alimentary tract, 154 females with breast carcinoma). (See also CRA 1(2):#287, 1963.)

- 64-1204 HODGKIN'S DISEASE AT 83. (E., Abstract) Howell, T. H. (St. John's Hosp., London, S.W. 11). *Brit. Med. J.* 1:1117, 1964.

An 83-year-old woman with few physical findings was found at autopsy to have lymph nodes, liver and spleen histologically typical of Hodgkin's disease, which is rarely found among the elderly.

- 64-1205 HISTOGENESIS OF THE CLEAR-CELL SKIN EPITHELIOMAS. (Rus.) Gubareva, A. V. (Centl. Res. Inst. Med. Radiol., Leningrad). *Ark. Pat.* 26(6):59-65, 1964.

Of 24 pts. with clear-cell skin epithelioma, only one was malignant. This tumor was located in the occipital region of a 32-year-old female. The examination showed marked cellular polymorphism, nuclear hyperchromatosis and increased mitotic and pathologic activity. Cellular polymorphism and increased mitotic activity were noted also in squamous cell structures, producing a picture similar to that of squamous cell cancer.

- 64-1206 SPONTANEOUS KIDNEY TUMORS IN DOMESTIC FOWL. (Fr.) Guillon, J.-C. (Lab. Diag. Res. Veterin. Med., Sanders Soc., Juvisy-sur-Orge (Seine-et-Oise), France), I. Chouroulinkov and L. Renault. *Bull. Assn. Franc. Cancer* 50(4):593-620, 1963.

Of 15,957 chickens of both sexes autopsied, 23 (0.14%) showed kidney tumors. The rate was 0.33% in those over 5 mo. of age, 0.25% in chicks younger than 5 mo., and non-significant in chicks younger than 4 wk. A relationship to sex or breed could not be established. The tumors did not favor any particular site; they affected both kidneys. Despite the diversity of histologic types, the tumors were of 2 types: those differentiated from tubules and those differentiated from the endothelium of the vessels. Despite their histological diversity, all tumors were of embryonic origin. They were identical in structure to the renal tumors obtained in fowl after inoc. with oncogenic viruses. It is therefore assumed that spontaneous and experimental tumors in fowl have the same etiology, and that the so-called leukemia viruses have an affinity to all undifferentiated elements of mesenchymal origin.

- 64-1207 INHIBITION OF GROWTH OF SUBCUTANEOUSLY IMPLANTED ASCITES TUMOR IN STRONG A MICE. (E.) Putong, P. B. (Dept. Path., Inst. Med., Far Eastern U., Manila), S. J. Juliano, O. C. Zuñiga, C. T. Triol and L. H. Panganiban. *J. Philipp. Med. Assn.* 40(2):114-121, 1964.

After pretreatment with $11.9-12 \times 10^6$ formalin-killed Ehrlich ascites tumor (EAT) cells in 0.2 ml, 1 inj./wk. for 3 wk. s.c. in the interscapular area, 72 male Strong A mice were challenged in wk. 4 with 2×10^6 live EAT cells in 0.2 ml doses and observed for 15 days. Controls were given 0.2 ml of normal saline soln. with 0.5% phenol and red cells previous to the live EAT cells. Inhibition of EAT growth was found in 20 mice (29.8%) of the pretreated group.

- 64-1208 DOUBLE CARCINOMA IN WOMEN. (Ger.) Schulz, H. (Clin. Surg., U. Jena, Germany) and G. Langer. *Arch. Geschwulstforsch.* 22(3):227-233, 1964.

In a period of 8 yr. (1954-1962), 18 pts. with double carcinomas were found in a series of 1730 carcinoma pts. examined. In 4 of these pts. (av. age 75.7 yr.) the 2 carcinomas were concurrent; the remaining 14 were an av. age of 53.6 yr. when the first carcinoma appeared and there was a lag of 1-24 yr. before the second appeared (av. interval was 8.5 yr.). Mammary and uterine carcinomas were most frequent, 9 and 7 cases, resp.

- 64-1209 ACUTE LYMPHATIC LEUKEMIA IN THE NEWBORN INFANT. AN ILLUSTRATIVE CASE. (It.) Pezzica, R. (Clin. Pediat., U. Turin, Italy). *Minerva Pediat.* 16(6):181-188, 1964.

The case history is presented of a 46-day-old girl with acute lymphatic leukemia. This report constitutes the fourteenth case reported in the literature and the first case in Italy of acute

lymphatic leukemia in newborn infants. Of the cases previously reported, 8/13 were of certain "congenital" nature and 5/13 were presumed "congenital". A 50% distribution occurred in both males and females.

- 64-1210 SARCOMA ON AN ULCER SCAR OF THE LEG. (Fr.) Degos, R., R. Touraine, J. Civatte, S. Belaich and J. Tinthoin. *Bull. Soc. Franc. Derm. Syph.* 70(5):815-817, 1963.

A 74-year-old woman, treated successfully 18 mo. previously with antibiotics for a common ulcer of the right leg, developed another ulceration at the scar site which showed a clinical picture of epitheliomatous degeneration. Bioptic examination resulted in a diagnosis of fibrosarcoma. The authors discuss the sarcomatous transformation of various skin conditions and the difficulty of a differential diagnosis with spinocellular epithelioma.

- 64-1211 TRAUMA AND SKIN CARCINOMA. (Ger.) Undeutsch, W. (Clin. Derm., U. Tübingen, Germany). *Berufsdermatosen* 11(5):245-258, 1963.

Malignant tumors due to trauma are extremely rare, as shown by the statistics on malignant degeneration of war injuries. A single mechanical injury followed by normal cicatrization virtually never produces a neoplasm. On the other hand, firm atrophic scars in areas exposed to considerable mechanical pressure are likely to ulcerate and eventually become malignant. As an example, the case of a 49-year-old male is presented, who suffered burns of the right leg, forearm, shoulder, and face at age 8.5; recurrent ulceration of the right patellar area finally led to a histologically confirmed squamous cell epithelioma. Another type of injury susceptible to malignant degeneration is the small, recurrent trauma, primarily that due to heat. The case of a blacksmith is cited, who repeatedly suffered burns on hands and forearms while working over an open fire; at age 69, he developed a prickle cell carcinoma on the dorsum of the left hand in the center of an atrophic, scarred and mottled area. Clinically and histologically, this lesion was very similar to radiation damage. Other cases are cited from the literature (30 references).

- 64-1212 A CASE OF CARCINOMA OF THE SKIN PRESUMABLY INDUCED BY TRAUMA TO A HEALED BURN SCAR. (Jap., Abstract) Koishi, T. (Natl. Maizuru Hosp., Japan), R. Daido and Y. Nakagawa. *Nippon Hifuka Gakkai Zasshi* (Jap. *J. Derm.*) 73(8):549, 1963.

A 54-year-old Oriental male who incurred a laceration from a hard blow in a healed burn scar on the scalp, developed approx. 2 yr. later spindle cell carcinoma. The original burn on the scalp was sustained at the age of 20 years and it took

approx. 7 yr. to heal, partly due to repeated trauma to the area.

64-1213 MULTIPLE NEVOID BASAL CELL EPITHELIOMAS, JAW CYSTS, AND SKELETAL DEFECTS. A CLINICAL SYNDROME. (E.) Maddox, W. D. (Mayo Clin., Rochester, Minn.), R. K. Winkelmann, E. G. Harrison, Jr., K. D. Devine and J. A. Gibilisco. *J.A.M.A.* 188(2):106-111, 1964.

A total of 2,725 case histories seen over a 32-yr. period (1930-61) with the diagnosis of basal cell epithelioma or epithelioma adenoides cysticum or both were reviewed at the Mayo Clinic, and 12 were found to have features of a syndrome including the above mentioned epitheliomas + jaw cysts and skeletal defects. In 4 illustrative case histories presented in detail, the pts. were seen 9-25 yr. before the disorder was considered serious in nature. Of the 12 with the syndrome, (6 men, 6 women; 12-69 yr. old), all had basal cell tumors; 11 had odontogenic cysts or tumors; 9 pts. had skeletal defects. Seven pts. had similar cutaneous disorders in the family. The 1 pt. without an odontogenic cyst or tumor had progeny with the syndrome, which had manifested itself in this family for 5 consecutive generations.

64-1214 RETICULOENDOTHELIAL SYSTEM AND NEOPLASMA. (E.) Ishibashi, Y. (Dept. Surg., U. Tokyo, Japan). *Tohoku J. Exp. Med.* 82(1):42-47, 1964.

Cancer pts. showed no change in serum properdin levels and were found to maintain the capacity of humoral antibody production fairly well after active immunization with tetanus toxoid even in later stages. Lower levels of antibody production to heterologous antigens after day 12 were observed in tumor-bearing mice as compared to normal mice. Delayed hypersensitivity tests showed that skin homografts from C57BL mice persisted much longer in ddD mice with Ehrlich carcinoma (21.4-day survival) than in those without (9.4-day survival). In humans, skin homografts in cancer pts. persisted much longer than in controls. Human cancer pts. subjected to the tuberculin test showed a delayed type of hypersensitivity. It is suggested that such a qualitative deficiency of the immune responses is responsible for the development and progression of neoplasm.

64-1215 NATURE OF THE TISSUE ANTIGEN OF RAT SARCOMAS PRODUCED BY HUMAN SARCOMA EXTRACT. (E.) Bashkayev, I. S. (Hertzen State Oncol. Inst., Moscow, USSR) and A. I. Ageenko. *Folia Biol. (Praha)* 10(3):159-163, 1964.

Specificity studies with adsorbed rabbit antisera showed that antiserum against rat tumor sarcoma 321 (initially induced by a human sarcoma) gave marked precipitation lines with tumor tissue only and did not react with normal rat tissue antigens. Experiments aimed at explaining the chemical nature of rat sarcoma antigens 321 and 358 by their serologic activity following pre-treatment with various enzymes showed the following: loss of serologic activity after treatment with papain, trypsin or diastase singly or combined; resistance to the action of lipase, DNase, RNase and hyaluronidase. Gel-diffusion precipitation tests with adsorbed antitumor serum showed clearly discernible precipitation lines with sarcoma 358 and sarcoma 321 antigens, but no reaction either with embryo antigens or with the antigens of adult rat organs. Antiserum against sarcoma 321 isolated from Wistar rats gave no precipitation lines with RNA and DNA preparations isolated from the tumor. (See also CRA 1(8):1625, 1963.)

64-1216 ALLERGY AND CANCER. (Ger.) Holler, G. (Alser Str. 27, Vienna). *Krebsarzt* 19(2):85-91, 1964.

Among 700 asthmatic pts. who became cured spontaneously or by corticoid therapy or specific desensitization, 19 (10 males, 9 females) subsequently developed malignant tumors of various types and locations. During the acute phase of lung allergosis, however, no malignant tumors were found. It is suggested that in the period after the cure of the allergy, the latent tumor growth becomes activated, particularly in persons with a hereditary predisposition to cancer.

64-1217 APPARENT CURE OF A JUVENILE ORBITAL RETICULUM CELL SARCOMA. (Fr.) Delthil, S., J. Sourdille and C. Haye. *Ann. Oculist. (Paris)* 197(5):491, 1964.

A case is presented of a 15-year-old girl with histologically confirmed reticulum cell sarcoma of the orbit, the apparent cure of which coincided with menarche at the age of 10; no recurrence has been seen since then. However, several remissions had occurred between ages 8 and 10 due to radiotherapy.

64-1218 BRONCHIAL CARCINOMA AND HYPERCORTICISM. (Ger.) Reichel, K. (Dept. Int. Med., City Hosp., Russelsheim/Main, Germany) and A. Moll. *Schweiz. Med. Wschr.* 94(31):1086-1087, 1964.

A case is presented of a 46-year-old man with metastasizing bronchial carcinoma and hypercorticism. So far 34 cases of this association have been published in the literature.

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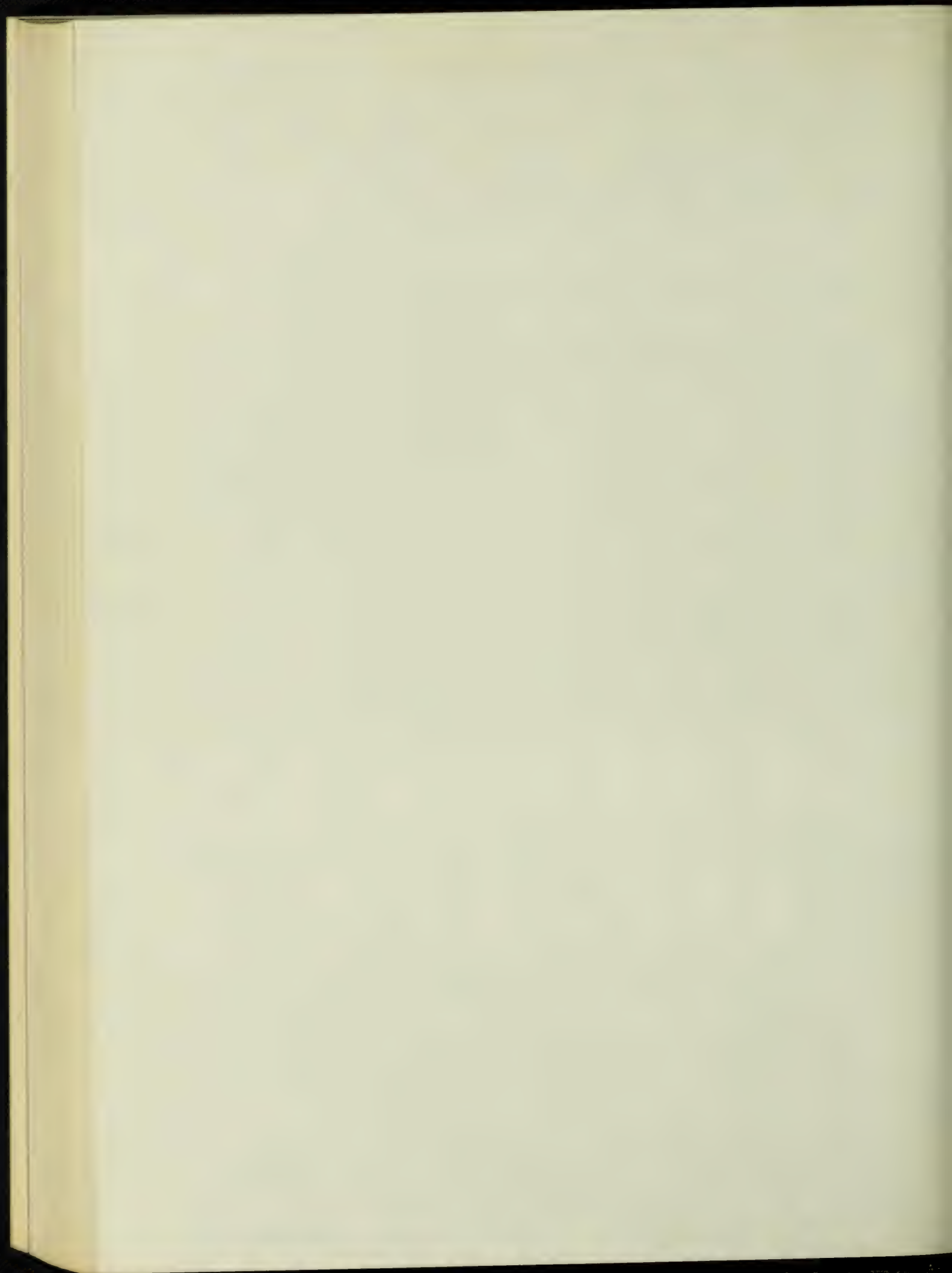
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CARCINOGENESIS

ABSTRACTS

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum, maximal
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubated(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	Ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

4-1219 SOME BIOLOGICAL EFFECTS OF AFLATOXIN. (E.) Carnaghan, R. B. A. (Centl. Veterin. Lab., Weybridge, England). Proc. Roy. Soc. Med. 57(5):414-416, 1964.

This review cites examples from the literature of the carcinogenic effect of peanuts and other foods infected with toxin-producing strains of *Aspergillus flavus* (toxic material collectively known as aflatoxin). The author reports that 1/37 ducks fed a ration containing 0.5% peanut meal (aflatoxin = 0.03 ppm) for 14 mo. developed hepatic tumors. The effect of aflatoxin on man is not known, but serious consideration should be given to the association of primary liver cancer and the presence of aflatoxin in foodstuffs. (8 references)

4-1220 POLYOMA VIRUS. A NEW TOOL FOR ONCOLOGIC INVESTIGATION. (Sp.) Estable, R. F. (NCI, Bethesda), A. S. Rabson and J. F. Estable-Puig. An. Fac. Med. Montev. (1-2):150-168, 1963.

Review is presented which discusses the carcinogenic activity of polyoma virus in the nervous system, tumors in various species, its ultrastructure, reaction to physical and chemical agents, its probable mechanism of action, and effect on cell cultures. (110 references)

4-1221 THE ENVIRONMENT IN RELATION TO CANCER. (E.) Wade, L. (Sloan-Kettering Inst. Cancer Res., New York). Med. Bull. Standard Co. (N. J.) 24(2):111-121, 1964.

Review article already abstracted as CRA 1(8):20, 1963 and *ibid.*, 2(4):#612, 1964 and which includes a reference to CRA 1(5):#839, 1963. (10 references)

4-1222 FETAL AND NEONATAL HAZARDS FROM DRUGS ADMINISTERED DURING PREGNANCY. (E.) Lan, S. Q. (Dept. Pediat., New York U. Sch. Med., N. Y.). New York J. Med. 64(4):493-499, 1964.

Review of transplacentally acquired agents which may produce neonatal morbidity or congenital malformations, teratogenic agents mentioned include endocrine preparations, cytotoxic antimetabolic agents, tolbutamide, and thalidomide. (31 references)

4-1223 FETAL IRRADIATION. (Fr.) Clavaud, P. Bull. Synd. Nat. Ginec. Obstet. Franc. (2):94-100, 1964.

Controlled studies on the incidence of leukemia and cancer in children born to mothers

who were irradiated during pregnancy are reviewed. The results generally indicate that X-ray doses in excess of 0.6 r increase the danger of leukemia or cancer, such as retinoblastoma, in the offspring, especially if the exposure occurs during the most active stage of embryogenesis. Utmost caution in the use of ionizing radiation for diagnostic purposes is therefore advised in cases of known or suspected pregnancy. (No references)

64-1224 GLOMUS TUMORS. (Fr.) Solal, C. Concours Med. 86(20):3237-3238, 1964.

In a brief review of the anatomic, physiologic, clinical and radiologic aspects of glomus tumors, the author reports that this condition arises more frequently in the middle aged and preferentially in women. Local trauma has been found to be an etiologic factor in 20% of the cases. (No references)

64-1225 THE THYMUS AND THE DEVELOPMENT OF IMMUNOLOGIC RESPONSIVENESS. THE THYMUS DIRECTS THE MATURATION OF IMMUNOLOGIC CAPABILITIES BY MEANS OF A HUMORAL MECHANISM. (E.) Miller, J. F. A. P. (NCI, Bethesda). Science 144(1):1544-1551, 1964.

An extensive review is presented of various factors involved in the development of immunologic responsiveness, especially the role of the thymus. Both experimental and clinical studies are cited. If C57BL mice, normally resistant to the oncogenic activity of polyoma virus, are thymectomized in the neonatal period, they become highly susceptible to the virus (inoc. of 2×10^6 PFU). Parotid tumors developed in 18/20 mice with an av. latent period of 69 days. In the 16 mice given virus and subjected to a sham operation, only 1 tumor developed, which had a latent period of 118 days. (See also CRA 1(9-10):#1713, 1964.) (Approx. 150 references)

64-1226 THOROTRAST TUMORS. QUANTITATIVE STUDIES ON THE DOSE-EFFECT PROBLEM IN THOROTRAST INTOXICATION. (Ger.) Wenz, W. (Dept. Surg., U. Heidelberg, Germany). Pp. 81-166 in Results of Surgery and Orthopedics (Ergebnisse der Chirurgie und Orthopaedie). Vol. 46. Bauer, K. H., A. Brunner and K. Lindemann (Eds.). Springer-Verlag (publ.), Berlin, 342 pp., 1964.

After a brief review of the literature on the induction of cancers by ionizing radiations, the relation of the dose of radioactive isotope to tumor production in experimental animals is discussed. The literature on the use of Thorotrast is then discussed in detail, including its distribution in the body and its excretion as well as its storage in various organs such as the spleen and liver. There is an extensive review of the

occurrence of tumors in man and experimental animals, taken from the literature, followed by a more detailed report on the quantitative relationships of the amount of Thorotrast, tumor frequency and latency derived from the author's work on rats. (430 references)

- 64-1227 EXPERIMENTAL TOBACCO CARCINOGENESIS. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York) and D. Hoffmann. Pp. 249-453 in Advances in Cancer Research. Vol. 8. Haddow, A. and S. Weinhouse (Eds.). Academic Press Inc., New York (publ.), 482 pp., 1964.

This extensive review on tobacco carcinogenesis involves not only historical aspects and objective of laboratory studies but also an interpretation of experimental findings and a postscript that indicates that perhaps, in terms of preventive medicine, efforts toward "modified" smoking products might benefit most people at the present time. Characteristics of tobacco and tobacco smoke are dealt with along with sampling techniques. A section deals with the yield of tobacco smoke condensate with the use of cigarette, cigar, pipe and oriental pipe. A large group of tobacco smoke constituents are discussed including polynuclear aromatic hydrocarbons, terpenes, phthalates, alkanes, heterocyclic nitrogen compounds, phenolic compounds and carboxylic acids, aldehydes and ketones, steroids, epoxides and lactones, nitrosamines, electric charge radicals and radioisotopes, arsenic and metallic constituents. An extensive table presents a selective summary of experimental work in reference to different body areas. (Approx. 700 references)

- 64-1228 IATROGENIC INJURIES. (Ger.) Lampert, F. (Child. Dept., U. Erlangen, Germany). Med. Klin. 59(25):1001-1008, 1964.

A review is presented of possible damage to the embryo caused by a wide variety of drugs taken during pregnancy or delivery; possible danger from electric pillows is also mentioned. Also presented are the possible effects of medications in mothers' milk upon the newborn. (130 references)

- 64-1229 PATHOLOGY AND SURGERY OF COLON CARCINOMA. (Ger.) Wittig, G. (Robert-Rossle Clin., German Acad. Sci. Berlin), W. Wirbatz and H. Berndt. Deutsch. Gesundheitsw. 19(19):845-851, 1964.

This review article discusses carcinoma of the large intestine (CLI) in youthful tumor bearers, relation between CLI and polyps, polyps in youths, intestinal polyposis, villous polyps, relation between CLI and ulcerative colitis, CLI and diverticulitis, and dissemination of CLI by 4 primary methods: infiltration into surrounding

organs, and hematogenous, lymphogenous tissue or spread by mechanical means. In one of 4 cases presented in detail, a 14-year-old girl had a family history of 5 relatives who died of intestinal and genital cancer. Of 336 of the authors' own cases with CLI, 6 also had ulcerative colitis (at av. age of 59 yr.). (No references)

- 64-1230 CHILDHOOD LYMPHOSARCOMA IN AFRICA. (Ger.) Oettgen, H. F. (Sloan-Kettering Inst. Cancer Res., New York). Med. Welt (29): 1553-1567, 1964.

A review of the epidemiology, etiology, clinical aspects, electron microscope findings, and therapy of maxillary lymphosarcoma in African children is presented. (29 references)

- 64-1231 CERTAIN ENVIRONMENTAL CONDITIONS AND HEMATOLOGICAL DISORDERS. (E.) Haurani, F. I. (Jefferson Med. Coll., Philadelphia, Pa.) and L. M. Tocantins. Arch. Environ. Health 8(6):778-804, 1964.

In an extensive review of the close relationship between environmental conditions and a wide spectrum of hematologic disorders, high altitudes, radiation and nutrition are chiefly considered. Leukemia seems to be the only latent manifestation of radiation among hematologic disorders; the latent period involved has been estimated to be between 3-5 yr. Up to 1959, there were 226 well-documented cases of leukemia (acute and chronic myeloid) from all over the world attributed to radiation. (354 references)

- 64-1232 EXPERIMENTAL INDUCTION OF CANCER WITH THE USE OF HUMAN ADENOVIRUSES. (Jap.) Yabe, Y. (Dept. Microbiol., Okayama U. Sch. Med., Japan). Saishin Igaku (Mod. Med. [Osaka]) 18(3): 607-612, 1963.

A review is presented of attempts to induce tumors in hamsters with human adenoviruses 2, 3, 7, 7a, 9, 10, 11, 12 and 14. Tumorigenic activity of Type 12 is further explored in its effect on cell cultures and subsequent inj. of cell-free filtrates into hamsters and the transplantability of some of the induced tumors. (25 references)

- 64-1233 CANCER AND NUCLEIC ACIDS. (Jap.) Sugimura, T. (Biochem. Div., Inst. Natl. Cancer Res. Ctr., Japan). Sogo Igaku (Medicine [Tokyo]) 20(12):861-866, 1963.

In this extensive literature review, the author discusses possible modes of action of carcinogens by their interaction with nucleic acids and subsequent induction of mutations in DNA structure. The importance of alkylation is stressed; quantum studies of various carcinogens are included. (32 references)

4-1234 RECENT STUDIES ON CARCINOGENESIS BY AIR POLLUTION. (Jap.) Mizutani, M. *J. Genet.* 38(1):77-87, 1963.

In an extensive review of the significance of air pollution in carcinogenesis, the author discusses various hydrocarbons found in exhaust concentrates and cigarette smoke condensates and their effects on mitosis and chromosome number in experimental studies with Chang's conjunctival cells and human lung cells. (56 references)

4-1235 COMPARATIVE STUDIES ON LEUKEMOGENESIS IN MICE INOCULATED WITH MURINE AND HUMAN LEUKEMIC MATERIALS. (E.) Sinkovics, J. G. (Dept. Med., U. Texas M. D. Anderson Hosp., Houston), C. C. Shullenberger and C. D. Howe. *Ad. Accad. Naz. Lincei* (65):171-184, 1964.

In an extensive review of leukemogenesis in mice, the authors classify the mouse leukemia viruses into thymic-lymphatic (Gross) and splenic-erythroblastic (Friend) types and report the differences in their biologic behavior. Electron microscope studies give evidence that virus particles, which may be maintained in tissue cultures derived from human leukemic organs, similar to mouse leukemia viruses do occur in the blood and tissues of leukemic pts. Massive trophic changes are not seen in these cultures, but delicate changes can be detected. The susceptibility of mice to human leukemia viruses is very low, and the transfer of human leukemia to mice have given mainly equivocal results. (4 references)

4-1236 THE RELATIONSHIP BETWEEN LUNG CANCER AND PULMONARY TUBERCULOSIS. (Jap.) Mori, S. (Osaka Pref. Ctr. Adult Dis., Japan). *Japan Kyobu Rinsho* (Jap. J. Chest Dis.) 22(7):443, 1963.

In a discussion of experimental studies, most of which already were reported, dealing with tumor inhibition and increased survival time obtained by the admin. of various vaccines (BCG and others) in mice with INH-induced lung adenomas, the author reviews the literature with regard to coexistence of pulmonary tuberculosis and lung cancer. Clinical incidence was found to be higher than autopsy incidence. It is concluded that the two forms are independent and that further investigation is needed, based on autopsy findings. (9 references)

4-1237 THE URGENT NEED FOR EPIDEMIOLOGIC STUDIES IN CANCER RESEARCH. A DEFINITION OF THE EXTENT AND CURRENT STATUS OF EPIDEMIOLOGIC STUDIES IN CANCER RESEARCH. (Ger.) H. Rössle (Robert-Rössle Clin., German Acad. Sci., Berlin). *Deutsch. Gesundh.* 19(22):985-991, 1964.

In a general review, the author discusses methods, potential possibilities, and limitations of epidemiologic research studies, as well as the current situation with respect to such studies in the German Democratic Republic. In reference to lung cancer and smoking habits, he comments that the most important argument against accepting the existence of a causal relationship is found in the faulty methodology employed in most or all of the allegedly confirmatory studies, to date, including exclusion of obviously important variables, the use of inadequate controls, comparisons of data which do not have a common base, etc. He concludes that it would appear, in the light of present knowledge, that bronchogenic carcinoma results from the combined effect of a number of etiologic factors, involving both endogenous and exogenous considerations, and that cigarette smoking is not only not the sole cause of the disorder, but possibly not even the most important one. (27 references)

64-1238 GERMFREE ANIMALS AND BIOLOGICAL RESEARCH. (E.) Pollard, M. (Lobund Lab., U. Notre Dame, Ind.): *Science* 145(2):247-251, 1964.

The author discusses the use of germfree (axenic, gnotobiotic) animals in various areas of biologic research, such as virology, oncology, virus induction of tumors, radiation leukemia, and other studies. (See also CRA 2(2):#287; *ibid.*, (5):#889; and *ibid.*, (6):#1049, 1964.) (33 references)

64-1239 CONGENITAL LEUKEMIA AND GENETICS OF LEUKEMIA. (Jap.) Miwa, T. (3rd Dept. Int. Med., U. Tokyo Sch. Med., Japan) and K. Kinugasa. *Igaku (Medicine)* 20(8):549-554, 1963.

In this literature review, the authors discuss the incidence of congenital leukemia, its familial relationship with leukemia and other malignancies, its cytological makeup (abnormal chromosome forms and number) and its association with Down's syndrome. (69 references)

64-1240 TRANSMISSIBLE MOUSE LEUKEMIAS AND FRIEND'S DISEASE. (Fr.) Ravina, A. *Presse Med.* 72(14):827-830, 1964.

In a review of published studies on induction of myeloid leukemias in newborn mice by cell-free filtrates of murine sarcomas and epitheliomas, and on the closely related Friend's disease, the following conclusions were drawn. The sensitivity of animals to tumorigenic viruses decreases with age. Some of these viruses are antigenic, others are not, at least not in the species where they are carcinogenic. There are several intermediate forms between infectious and carcinogenic viruses; some may be infectious in one recipient, carcinogenic in another, or they may be both at the

same time. From the therapeutic point of view, it is significant that effective vaccines against leukemogenic viruses have been prepared. However, the fundamental problems of the pathogenesis of leukemias still remain to be solved. (9 references)

- 64-1241 AETIOLOGY OF CENTRAL AFRICAN LYMPHOMATA. (E.) Harris, R. J. C. (Imperial Cancer Res. Fund, London). Brit. Med. Bull. 20(2):149-153, 1964.

The author discusses the Burkitt tumor with regard to its high incidence in children, its relation to age and anatomical distribution. Of considerable value from the point of view of etiology is the finding that altitude, temperature and annual rainfall are more directly implicated than racial distribution. After a review of viruses and tumors in man, it is concluded from more recent experimental investigations that the tumor probably results from a bizarre host reaction towards a common arthropod-borne virus or group of arthropod-borne viruses. A virus-carcinogen interaction is also considered. (51 references)

- 64-1242 CONTEMPORARY STATE OF THEORIES ON THE ETIOLOGY OF LEUKEMIA. (Bul.) Georgiev, Z. Suvr. Med. (Sofia) 15(2):31-39, 1964.

This review on the etiology of leukemia includes discussions on the viral theory, genetic characteristics, theory of immunology and enzymatic disturbances. The role of viruses, ionizing radiation, chemicals, bacteria, and other factors is also mentioned. All of the above factors may be responsible for the occurrence of cellular mutations resulting in selective proliferation leading to neoplastic or leukemic processes. (66 references)

- 64-1243 A VIRUS IN EXPERIMENTAL TUMORS WHICH INCREASES LACTIC DEHYDROGENASE. (Ger.) Georgii, A. (Path. Inst., U. Munich, Germany). Klin. Wschr. 42(12):559-563, 1964.

A previously reported virus or virus-like substance demonstrated in mouse ascites Sarcoma I (see CRA 2(3):#521, 1964), which increases serum lactic dehydrogenase (LDH) without appearing to exert any significant pathogenic effect on the organs or tissues of the animal, is now believed to be the same agent as that described by Riley et al. and to be definitely viral in origin. In the present review of the literature, its presence appears to be confirmed in at least 36 different types of transplantable mouse tumor, AKR mouse leukemia induced by transplant (but not in that arising spontaneously), Moloney virus leukemia (except that induced by tissue culture trans-

plants) and other transplantable mouse leukemias, including L 1210. It has not been demonstrated in mouse tumors induced by polyoma virus, in transplantable rat tumors, or in human malignancies. The author suggests that the presence of this LDH-stimulating agent may be taken as a positive evidence of viral infection, although the question of its exerting a stimulating or synergistic effect on tumor growth continues to be unresolved. (48 references)

- 64-1244 LIVER TUMOURS IN CAPTIVE BEARS. (E.) Editorial. Lancet 1:1429, 1964.

Carcinoma of the liver was reported in 7 bears in the San Diego Zoological Gardens; 5/7 lived in the same enclosure most of their lives (see CRA 2(5):#956, 1964). Only six such tumors were previously reported; none were observed in 87 necropsies on bears in the Philadelphia Zoological Gardens between 1901 and 1955. This brief review indicates that further investigations in captive species may be helpful in cancer research. (4 references)

- 64-1245 EFFECTS OF CHEMICAL CARCINOGENESIS ON THE STRUCTURE AND METABOLISM OF NUCLEIC ACIDS. (Cz.) Sula, J. (2nd Inst. Chem., Charles U. Sch. Med., Prague, Czech.). Cas. Lek. Cesk. 103(15):406-412, 1964.

A review is presented of mutation theories of carcinogenesis which involve the nucleic acids of the cell. Chemical, physical, or viral agents are discussed which may bring about changes in the genetic material of the cell by alteration of this material or even by introduction of foreign, i.e., viral, genetic material into it. (55 references)

- 64-1246 CAUSES OF CONGENITAL MALFORMATIONS. (Ger.) Widok, K. (Dept. Urol., U. Homburg/Saar, Germany) and H. Widok. Hippokrates 35(11):417-424, 1964.

A review is presented on causes of malformations, including hereditary, endogenous and exogenous factors, chemical noxae, environmental factors, nutritional deficiencies, infectious diseases (particularly viral), irradiation, hormonal factors, maternal age, and mechanical injury. (82 references)

- 64-1247 ON THE VIRAL ETIOLOGY OF CANCER. (Hun.) Zilber, L. A. (Acad. Med. Sci. USSR, Moscow). Orv. Hetil. 105(22):1009-1014, 1964.

A review of the author's work and that of others presented at the meeting of The Hungarian Academy of Science, August 28, 1963. Content is basically identical with that abstracted in CRA 1(7):#1213, 1963. (No references)

See also abstract no: 1344

PHYSICAL CARCINOGENESIS

1248 RADIATION-INDUCED MOUSE LEUKEMIA: CONSISTENT OCCURRENCE OF AN EXTRA AND A MARKER CHROMOSOME. (E.) Wald, N. (U. Pittsburgh Sch. Med., Pa.), A. C. Upton, V. K. Jenkins and W. H. Borges. *Science* 143(1):810-813, 1964.

extra chromosome and an abnormal marker chromosome were frequently found in the marrow cells of Up mice (both sexes) that developed leukemia after inoc. (i.v.) with cell-free plasma or spleen ultracentrifugates or spleen cells from transfer recipients 21-27 of mice with a radiation-induced granulocytic leukemia. The "marker" chromosome was seen in both sexes and did not resemble the Y chromosome. It was in the size range of 13th to 16th pairs. The marker was seen in the highest frequency in cells having 41 chromosomes.

1249 GENERALIZED HYPEROSTOSIS INTERNA AND OSTEOSARCOMAS IN TOTAL BODY X-RAY IRRADIATED FEMALE SWISS ALBINO MICE WITH HORMONALLY INDUCED OVARIAN TUMORS. (Ger.) Cottier, H. (Inst. Path., U. Bern, Switzerland), H. Keller and B. Roos. *Path. Microbiol. (Basel)* 27(4):466, 1964.

Previous studies showed that total body irradiation (TBI) caused female Swiss albino mice to develop ovarian tumors, and most of them to also develop a generalized hyperostosis interna (GHI). These effects occurred about 10 times more frequently after TBI than in non-irradiated mice; present in non-irradiated mice both effects developed 10-25 mo. later than in irradiated mice. Studies in mice of both sexes, osteogenic sarcoma developed only in irradiated females with ovarian tumors and GHI. It was found that in female Swiss albino mice with ovarian tumors and which had at the age of 3 mo. a single total X-ray irradiation and were sacrificed or at age 4-30 mo., the appearance of osteogenic sarcomas correlated well with the intensity of biologic signs of continuous and hyperestrogenic ($P < 0.05$), but no correlation could be established with the extent and signs of continuous hyperandrogenism.

1250 RADIUM-226, RADIUM-228, LEAD-210, AND FLUORINE IN PERSONS WITH OSTEOGENIC SARCOMA. (E.) Lucas, H. F., Jr. (Argonne Natl. Lab., Ill.), R. B. Holtzman and D. C. Dahlin. *Science* 144(1):1573-1575, 1964.

Comparison of accumulated absorbed dose in bone of naturally occurring radioisotopes Ra^{226} , Ra^{228} , and Pb^{210} of normal persons to that of persons with proven osteogenic sarcoma showed no significant differences. This was equally true for the bone conc. of 2 stable bone-seeking elements, fluorine and lead. The environmental concentrations of these elements seemed to be the determining factor in bone conc., irrespective of bone

condition. Analyses were made from bone specimens removed for treatment of 32 pts. (19 males); histologic types included osteoblastic, chondroblastic and fibroblastic sarcomas. Severity of malignancy ranged from Grade 1 to 4.

64-1251 CANCER IN THE RAT AFTER SINGLE EXPOSURES TO IRRADIATION OR HYDROCARBONS. AGE AND STRAIN FACTORS. HORMONE DEPENDENCE OF THE MAMMARY CANCERS. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.) and R. Fukunishi. *Radiat. Res.* 20(3):493-503, 1963.

The influence of racial strain on the incidence of cancer was demonstrated by the fact that following single doses of X-rays (400 r) admin. between age 3-52 days, among 146 Sprague-Dawley (SD) rats that survived 6 mo., 24.7% developed mammary tumors and 5.5% developed sarcomas after 84-184 days, while in 71 Long-Evans rats only 2 sarcomas developed (2.8%; latent period 159 and 166 days). After single irradiation on day 52, SD rats showed the following: mammary carcinoma incidence of 29.7%; 92% of cancers detected within 79 days; multiple carcinomas in 13%. In 57 sisters given 2 irradiations (each 400 r) at 52 and 92 days, 60% showed mammary carcinomas (25-220 days); 27% had multiple carcinomas. One rat in this group developed a fibrosarcoma. After i.v. admin. to 34 SD rats of 9,10-dimethyl-1,2-benzanthracene (DMBA; 5 mg), mammary carcinoma incidence was 100%, latent period was 27-48 days and multiple incidence was 68%. Mammary carcinomas in SD rats, either DMBA- or X-ray-induced, shared the following properties: similar histologic appearance; similar regression after ovariectomy; similar content of pyridine nucleotide-linked dehydrogenases (glucose-6-phosphate, 6-phosphogluconic, isocitric, lactic and malic).

64-1252 THYROID CANCER DEVELOPING AFTER IRRADIATION OF THE ADULT. (E.) Hynes, J. F. (St. Francis Hosp., Wilmington, Delaware). *Delaware Med. J.* 36(6):124-126, 1964.

The case is presented of a man who developed multiple adenomata and a small focus of papillary carcinoma in the thyroid 10 yr. after receiving X-ray therapy (about 1,500 r in each lobe) for Hodgkin's disease localized in the neck and mediastinum.

64-1253 PLUTONIUM INHALATION STUDIES--VI. PATHOLOGIC EFFECTS OF INHALED PLUTONIUM PARTICLES IN DOGS. (E.) Clarke, W. J. (Biol. Lab., Hanford Lab., Richland, Washington) and W. J. Bair. *Health Phys.* 10(6):391-398, 1964.

The inhalation of $Pu^{239}O_2$ aerosol by beagle dogs caused spontaneous death (55-855 days post-exposure) in those having a lung burden of 2-48 μC . The body burden of Pu at 30-384 days post-exposure

was 95% for lungs and 4% for bronchial and mediastinal lymph nodes. Although primary lung cancer was not found in the radiation damaged lungs, many of the proliferative changes that occurred were similar to precancerous lesions: alveolar septal cell proliferation, vascular fibrosis, alveolar and squamous metaplasia, development of elastotic collagen in lung scars, blockage of lymphatic channels and progressive lymphopenia. (See also CRA 2(3):#436, 1964.)

- 64-1254 THOROTRAST TUMOURS. REPORT OF 3 CASES AND A MICRORADIOLOGICAL STUDY OF THE DEPOSITION OF THOROTRAST IN MAN. (E.) Hassler, O. (Dept. Path., U. Umeå, Sweden), K. Boström and L.-O. Dahlbäck. Acta Path. Microbiol. Scand. 61(1):13-20, 1964.

After a long latent period of 21-27 yr., 3 male pts. (age 47-74 yr. at death), who had been inj. with Thorotrast (T; 17 ml, 30 ml and an unspecified amount) to obtain cerebral angiographs, developed liver tumors (2 adenoacanthomas and 1 hemangioendothelioma). Microradiograms made at autopsy clearly depicted T in tumorous liver and spleen tissue as granular pigment. Solitary small granules of radiopaque material were also found in bone marrow and lymph nodes.

- 64-1255 CASE REPORT OF CARCINOMA OF THE SKIN INDUCED BY LONG-TERM USE OF A DEVICE WITH A MINIMAL DOSE OF RADIOACTIVE SUBSTANCE. (Jap.) Iga, M. (Nagoya Municipal Coll., Japan), T. Abe and H. Kanno. Nippon Hifuka Gakkai Zasshi (Jap. J. Derm.) 73(8):558-559, 1963.

In the home treatment of abdominal pain and neuralgia, a 61-year-old Oriental man applied for 24 yr. to the back and abdominal regions a radium-containing plate, calculated to have emitted a total dose of 1,000-6,000 r within that period. Four yr. previously, pigmentation and papules appeared on the skin of the abdomen and back, and multiple ulcers or small tumors then developed. Histopathological studies revealed a carcinoma of the skin and various transitional stages ranging from chronic radiation dermatitis to carcinoma.

- 64-1256 LEUKAEMOGENIC EFFECT OF IONISING-IR-RADIATION TREATMENT IN POLYCYTHAEMIA. (E.) Modan, B. (Johns Hopkins U. Sch. Hygiene Public Health, Baltimore, Md.) and A. M. Lilienfeld. Lancet 2:439-441, 1964.

In a preliminary study of pts., aged 35 yr. or more when diagnosed as having polycythemia vera, it was found that 7/79 (8.9%), 25/228 (11%), and 12/72 (16.7%) who were treated with X-rays alone, P32 or P32 + X-rays, resp., developed acute leukemia. Of pts. who had not been treated with either form of radiation, only 1/133 developed leukemia. Acute leukemia developed in 2/73, 6/69, 6/40 and 11/45 pts. treated <2 to >12 yr. with P32 in total doses of 1-9, 10-19, 20-29 and 30 or more mC, resp. Incidence of acute leukemia in 102 pts. with questionable polycythemia treated with P32 was 9.8%; after X-rays + P32 incidence was 8% of 25 cases. The increase in survival time resulting from treatment did not appear to be a significant factor in leukemogenesis.

- 64-1257 A COMPARATIVE STUDY OF THE EFFECTS OF IMBEDDING CELLOPHANE AND POLYSTYRENE FILMS IN RATS. (E.) Oppenheimer, E. T. (Inst. Cancer Res., Coll. Physicians Surgeons, Columbia U., N. Y.), M. Willhite, A. P. Stout, I. Danishefsky and M. M. Fishman. Cancer Res. 24(3):379-387, 1964.

Cellophane was implanted abdominally s.c. in 3 groups of male Wistar rats. As in a previous study with polystyrene, when the induced envelop + the film was removed at monthly intervals, no tumors developed; when only the film was removed there was a decrease in the number of tumors produced compared to those in which film and pocket remained *in situ* throughout the period of observation. With cellophane, histological studies showed a much greater fibroblastic activity and a shorter contact time necessary for initiating neoplastic changes (3 mo. compared to 6 mo. for polystyrene). Another difference related to cellophane is its marked tendency toward calcium deposition in pockets, in tumors, and on the film itself.

See also abstract nos.: 1223, 1226, 1242, 1245, 1246, 1258, 1333

CHEMICAL CARCINOGENESIS

1258 ELECTRON MICROSCOPIC STUDY OF VIRUSES OBSERVED IN MOUSE LEUKEMIA. (Abstract) Inoue, J. (Dept. Path., Tori U., Japan), K. Matsui and S. Moriwaki. Japan Ketsueki Gakkai Zasshi (Acta Hemat. Jap.) 3(4):387, 1963.

5/9 mice with variously induced leukemias, various viruses were detected in the lymph nodes of the spleen, regardless of the method used for induction of leukemia (testosterone, estradiol, castration, X-irradiation) or whether it was primary or transplanted leukemia. All of the viruses observed were identical and were the same as observed in lymphatic leukemia induced in the strain mice.

1259 EXPERIMENTAL INDUCTION OF RENAL NEOPLASMS. (Pol.) Wojewski, A. (Clin. Lab., Pomerian Acad. Med., Szczecin, Poland), J. Krasoń and R. Roessler. Pol. Przegl. Chir. 19(4):583-589, 1964.

Twenty white male rats (5-7 mo., wt. 150-250 g) received 10 mg of methylcholanthrene (MC) and 10 unselected male rabbits (4-5 mo.) received 10 mg of MC. Half of each species received the MC (surgically introduced) into the parenchyma of the lower pole of the kidney (LPK) and half into the renal pelvis (RP); they were observed for 12 mo. In survivors, squamous cell carcinoma developed in 3/10 RP rats; only benign cysts developed in 6/10 rats and 3/10 LPK rabbits. No tumors occurred in the remaining group of 10 rabbits. It was concluded that rat kidney is more sensitive to MC than the rabbit kidney. Direct contact of MC with the mucosa of RP for at least 6-12 mo. seemed to be a prerequisite for carcinogenesis.

1260 CARCINOGENIC ACTIVITY OF AFLATOXIN TO RATS. (E.) Barnes, J. M. (Toxicol. Unit, Med. Res. Council Lab., Carshalton, Surrey, England) and W. H. Butler. Nature (London) 202:1016, 1964.

Aflatoxin (AF; Af B₁ and G₁ mostly; in arachis oil) was fed to 7 rats for 89 days at a final conc. of 10 ppm in a diet that produced no liver changes in control rats. At 89 days, 1/7 was sacrificed and showed a liver with the normal lobular pattern, no ill-defined hyperplastic nodules and a few parenchymal cells with hyperplastic nuclei. Following AF treatment, 3/7 were returned to the normal diet for 316-485 days; at autopsy all 3 had multiple hepatocarcinomas; one of these had multiple small pulmonary metastases. After 15 days of normal diet, 3/7 rats received a second dose of AF for 7-220 days. Seven days after the last AF, the liver of one was normal; after 15 days, the liver of a second rat showed hyperplastic cells but no regenerative nodules;

after 220 days followed by 96 days of normal diet the liver of the third rat had a large hepatocellular carcinoma. It was calculated that the carcinogenic dose of AF for rats is not greater than 2.5 mg/rat. (See also CRA 2(2):#241, 1964.)

64-1261 RESULTS OF INTRACEREBRAL APPLICATION OF METHYLCHOLANTHRENE IN MICE. (Fr.) Van Haelst, U. J. G. M. (Fac. Med., U. Nijmegen, The Netherlands) and G. J. V. Swaen. Bull. Assn. Franc. Cancer 50(4):659-669, 1963.

Methylcholanthrene pellets, wt. approx. 1 mg, were introduced in the left cerebral hemisphere of 77 young adult C3H mice (37 males, 40 females); 65 of the mice belonged to the subline C3H₂, 12 to the subline C3H_f. A total of 23 tumors was obtained: 16 sarcomas of the head (predominantly fibrosarcoma), 3 cerebral tumors (2 astrocytomas, 1 oligodendroglioma), 3 mammary epitheliomas, and 1 osteogenic sarcoma of the back. The 2 latter types occurred in C3H₂ mice and were considered spontaneous. The rate of sarcomas of the head and of cerebral tumors was 20% and 3%, resp., in C3H₂ mice; 25 and 8%, resp., in C3H_f mice. The average interval between pellet implantation and appearance of the tumors was 261 days for the sarcomas and 346 days for the brain tumors.

64-1262 THE ULTRASTRUCTURE OF BERYLLIUM-INDUCED OSTEOGENIC SARCOMA IN THE RABBIT. (E., Abstract) Peterson, L. F. A. (Mayo Clin., Rochester, Minnesota), A. L. Brown and J. M. Janes. J. Bone Joint Surg. (Am.) 46-A(4):920, 1964.

While the cells of beryllium-induced sarcomas in rabbits showed considerable variation in size their intracellular content resembled that of normal osteoblasts. Multiple nuclei or nucleoli or large numbers of mitochondria were observed in some cells, while others showed eccentrically located nuclei. Cytoplasm and endoplasmic reticulum were within normal limits. The matrix showed normal collagen cross-banding, but the fibrils varied in thickness and were randomly arranged. No evidence of intracellular zinc beryllium silicate particles was found.

64-1263 AUTOLOGOUS AND HOMOLOGOUS TUMOR TRANSPLANTATION IN ANIMALS BEARING METHYLCHOLANTHRENE-INDUCED SARCOMA. (E.) Matsuyama, M. (2nd Dept. Path., Nagoya City U. Sch. Med., Japan). Gann (Jap. J. Cancer Res.) 55(3):237-243, 1964.

Essentially similar to CRA 1(3):#397, 1963, and ibid., 2(3):#489, 1964.

64-1264 BASIC AND CLINICAL STUDIES OF MALIGNANT TUMORS. (Jap.) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan). Shindan To

Chiryo (Diag. Ther. [Tokyo]) 51(7):1229-1232, 1963.

See CRA 2(2):#248; and *ibid.*, #249, 1964 and earlier papers for studies on 20-methylcholanthrene-induced leukemias in RF mice.

64-1265 HISTOGENESIS OF LUNG CARCINOMA IN MICE INDUCED BY 4-NITROQUINOLINE 1-OXIDE: CARCINOMA ARISING FROM AREAS OF ADENOMA. (E.) Mori, K. (Dept. Med. Zool., Showa Sch. Med., Tokyo, Japan) and I. Hirafuku. *Gann (Jap. J. Cancer Res.)* 55(3):205-209, 1964.

See CRA 1(4):#624, 1963.

64-1266 ALLOOCIMENE: ABSENCE IN CIGARETTE SMOKE. (E.) Mold, J. D. (Dept. Res., Liggett Myers Tobacco Co., Durham, N. C.), T. B. Walker and J. B. Williams. *Science* 144(1):1572-1573, 1964.

Determinations from gas chromatograms of volatile extracts of the smoke of 2 blends of cigarettes (Bright (flue-cured) and a commercial blend of Bright, Burley, Turkish and Maryland), a technic shown to have a recovery efficiency for alloocimene of 86%, indicated that alloocimene was essentially absent from the smoke condensate (0.006%). During these tests, the presence of dipentene was confirmed; it represented 0.2-0.3% of the smoke condensate from both types of tobaccos.

64-1267 THE EFFECT OF URETHANE ON MITOTIC CELLS OF MICE OF DIFFERENT AGES AND STRAINS. (E.) Wakonig-Vaartaja, R. (Dept. Obstet. Gynec., U. Adelaide, S. Australia). *Aust. J. Exp. Biol. Med. Sci.* 42(Pt. 2):165-172, 1964.

The spleen and bone marrow tissues of mice inj. s.c. with urethan (1 mg/kg, a tumor-initiating dose) showed abnormal metaphases which decreased in number with increasing age of the mouse and with increase of interval following the drug; the chromosomal abnormalities also varied widely among the 4 strains used. Gowan A strain mice showed the greater sensitivity to urethan with 41.9% abnormal metaphases in bone marrow and 55.8% in spleen after 24 hr.; for other strains comparable figures were, resp., A, 19.5% and 20.3%; C3H, 17.9% and 31.0%; E x H, 15.8% and 14.2%. The estimated mitotic index in the spleen of mice of different ages showed a marked decline from 2-12 days of age after which it remained at a constant level. The number of chromatid breaks per cell declined with age of host and with time after treatment.

64-1268 HISTOCHEMICAL STUDIES OF URETHAN-INDUCED LUNG ADENOMAS IN MICE. (Rus.) Uzunov, P. V. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci.

USSR, Moscow). *Vop. Onkol.* 10(6):72-78, 1964.

After admin. of urethan (U; 20 mg every 5 days x 6, total 120 mg, i.p.) to 50 Strain A mice (males, females), all showed lung adenomas when sacrificed after 1-6 mo.; 1/8 controls developed a spontaneous adenoma. A malignant adenoma developed in a mouse after 5 mo. Histochemical examination showed high activity of succinic dehydrogenase and cytochrome oxidase in the lung adenomas which was similar to that in bronchial and bronchiolar epithelium as well as to that in the proliferative zones of bronchogenic epithelium. RNA gradually increased during carcinogenesis, and was most pronounced in differentiated adenomas; the increase in DNA was insignificant. There was also a gradual increase in lipid dystrophy in the cells of pulmonary adenomas. Therefore, the morphological and especially histochemical data indicate the bronchogenic origin of lung adenomas in mice treated with U.

64-1269 TERATOGENIC ACTIVITY OF NIAGARA BLUE 2B AND AFRIDOL BLUE. (E., Abstract) Lloyd, J. B. (Dept. Biochem., University Coll., Cardiff, England) and F. Beck. *Biochem. J.* 91(2):14P-15P, 1964.

At day 8.5 of pregnancy, inbred Wistar rats were inj. s.c. with 1% aqueous soln. of Niagara blue 2B or Afridol blue and were sacrificed at day 20.5. With Niagara blue 2B, the number of mothers (M), the number of implantations (I), resorptions (R) and abnormal fetuses (A) were 9, 86, 5.8% and 1.2%, resp., for doses of 50 mg/kg; 8, 77, 19.5% and 3.9%, resp., for 100 mg/kg; 6, 58, 29.3% and 13.8%, resp., for 150 mg/kg; 3, 33, 100% and 0%, for 200 mg/kg. Results for Afridol blue (50 mg/kg) were M, 10; I, 101; R, 30.7%; A, 8.9%. It appears that a number of dyes besides trypan blue (see CRA 2(2):#267, 1964) have a teratogenic effect upon rats.

64-1270 VINBLASTINE. (E.) Cohan, S. Q. (Dept. Pediat., New York U. Sch. Med., New York), J. Dancis and D. Kitay. *Lancet* 1:1390, 1964.

The fetuses of rats and mice given vinblastine in the last third of pregnancy showed thereafter a significant increase of mitotic figures over those in fetuses of controls. Vinblastine (0.12-0.30 mg/kg, i.p.), admin. to 94 pregnant rats from day 7 to day 12 of gestation, caused total litter resorption in 56 (60%). Among 38 litters which came to term, 24/304 young (8%) showed gross developmental anomalies, including stunting, exencephaly, iniencephaly, rachischisis, gastroschisis, and malformation of the lower extremity.

64-1271 SELECTIVE INDUCTION OF NASAL CAVITY CARCINOMAS IN RATS BY N,N'-DINITROSOPIPERAZINE, NITROSOPIPERIDINE, NITROSOMORPHOLINE,

ETHYLALLYL-, DIMETHYL- AND METHYLVINYLNITROS-
AMINE. (Ger.) Druckrey, H. (Dept. Surg.,
Freiburg i. Br., Germany), S. Ivankovic, H. D.
ennel and R. Preussmann. *Zschr. Krebsforsch.*
66(2):138-150, 1964.

After treatment with dinitrosopiperazine (DP;
10 mg/kg x 1-2/wk., s.c.), 10/13 BDII (albino) or
(black) rats developed ethmoid carcinomas, 6
rats simultaneously showed papillomas and 1 car-
cinoma of the esophagus; 1/13 had only esophageal
cancer. Nitrosopiperidine (NP; 10 mg/kg x 2/wk.,
s.c.) was admin. to 25 BDII, IV, or VI rats; 20
showed ethmoid carcinoma and 2 had benign tumors
(cholesteatoma) of the sinus; 5 also had papil-
omas, 8 had multiple carcinoma of the esophagus,
others had only esophageal cancer and 1 only
papillomas. Average carcinogenic total dose
(TD), and av. induction time (IT) for DP or NP
were, resp., 1086 or 900 mg/kg, and 526 or 366
days. N-Nitrosomorpholine (NM; 5 or 10 mg/kg
/wk., i.v.) produced liver cancer in 2 rats,
1 carcinoma of ethmoid cells in 5 other rats;
IT = 400-450 days. Similar tumors were observed
after i.v. admin. of N-methyl-N-allyl-nitros-
amine (NMN; 10 or 20 mg/kg/wk., i.v.) which led
to nephroblastomas. In inhalation studies, BDII
rats were exposed to N,N-dimethylnitrosamine
(DMA; 1x/wk. for 30 minutes = 7.5 mg/kg) and
died between day 230-470 showing extensive car-
cinoma of the ethmoturbinal region. In another
experiment, DMNA (50% of above conc.) produced
extensive ethmoid-cell carcinomas in 9/12 rats;
IT = 260-450 days. No other tumors were ob-
served. Of 12 rats exposed to N-methyl-N-vinyl-
nitrosamine (MVNA; 2.7 mg/kg x 1/wk. for 30 min.),
died between day 230-330 showing destructive
squamous epithelium carcinoma of the nasal cavity.
In contrast to the other experiment, these tu-
mors did not originate in the ethmoid cells but
were found exclusively in the region of the
anterior nasal cavity. After p.o. admin., MVNA
in all cases caused squamous epithelial carci-
noma of the pharynx and esophagus, but not of
the nasal cavity.

1272 MORPHOLOGY OF KIDNEY TUMORS IN THE RAT.
(Ger.) Thomas, C. (Inst. Path.,
Mannheim, Germany) and D. Schmähl. *Zschr.*
Krebsforsch. 66(2):125-137, 1964.

Rats treated with various nitrosamines and nitros-
amines developed kidney tumors which were epi-
thelial or mesenchymal neoplasms. Dimethyl-
nitrosamine (D; 30 mg/kg x 1; inhaled) caused a
nephroblastoma in one rat; nitrosoethylurethan
(E; 50 mg/kg/wk., i.v.) produced a cystic-papil-
lary carcinoma of the cortex with metastases to
lymph nodes and cervical lymph nodes in another rat.
Renal kidney tumors originated usually in the
cortex, and rarely in the medulla or renal
pelvis; histologically they were adenomas, carci-
nomas or cystomas. Macroscopically and histolog-
ically, the mesenchymal tumors resembled Wilms'
tumor in man. A correlation between the tumor

localization dosage and route of admin. of car-
cinogenic substances is tabulated from the liter-
ature (37 references). A comparison was made
between the epithelial and mixed tumors of the
nephroblastoma type and the spontaneous or in-
duced renal tumors noted in the literature. (See
also CRA 1(4):#665, 1963.)

64-1273 BINDING OF 2-AMINONAPHTHALENE TO DOG
BLADDER MUCOSA AND COMPONENT NUCLEO-
PROTEINS. (E., Abstract) Radomski, J. L. (Dept.
Pharmacol., U. Miami Sch. Med., Coral Gables,
Fla.) and E. Brill. *Fed. Proc.* 23(2)
(Pt. 1):281, 1964.

After single p.o. doses of 2-aminonaphthalene-
8-¹⁴C to dogs, max. activity in the bladder mu-
cosa of only 0.01% of the admin. dose was found
after 12-18 hr. Activity dropped off rapidly
thereafter. Activity was correlated with the
conc. of radioactive metabolites in the urine and
did not increase with repeated doses. When a
homogenate was examined spectrofluorometrically,
there was a definite fluorescence peak at 400 mμ
(340 mμ activation) which was not present in con-
trol mucosa.

64-1274 STUDIES ON THE REACTION OF THE SKIN OF
THE NECK OF CITELLUS RICHARDSONII
RICHARDSONII (SABINE), THE PRAIRIE GOPHER, TO
PAINTING WITH A 1% 3,4-BENZOPYRENE SOLUTION IN
ACETONE. (Ger., Abstract) Kaiser, H. E.
(1230 Decatur St., N.W., Washington, D.C.). *Zschr.*
Krebsforsch. 66(2):192, 1964.

In contrast to the mouse, the previously shorn
coat of a gopher regenerated despite 62 appli-
cations of a 1% 3,4-benzopyrene soln.; only a conc.
of pigment was found along with leukocytic in-
filtration. Macroscopic and histologic studies
revealed no precancerous state; only the coat
showed a minimal variation in color.

64-1275 EFFECT OF STEROIDS ON PRECANCEROUS
STAGES IN THE CERVIX. CONTRIBUTION TO
THE PROBLEM OF HORMONE FACTORS IN CARCINOGENESIS;
COLPOSCOPIC, CYTOLOGIC AND HISTOLOGIC OBSERVATIONS.
(Ger.) Hillemanns, H. G. (Cancer Cytol. Found.
Amer., Florida Div., Miami), J. E. Ayre and J. M.
Le Guerrier. *Arzneimittelforschung* 14(7):784-791,
1964.

Following a discussion and literature review (48
references) on steroid hormones and genital cancer
and carcinoma of cervix uteri, a possible acti-
vation of an already existing precancerous stage
during long-term therapy with Enovid (E; norethyno-
drel; 17α-ethynyl-17β-hydroxy-3-keto Δ⁵⁽¹⁰⁾-estren-
3-one + ethynylestradiol-3-methyl ether; 10 mg/day
p.o.) was studied in 112 pts. In the case of
normal or inflammatory cell findings without ana-
plastic nuclear tendency (among 50 pts.), no
changes occurred during or after therapy; in cases

with anaplastic nuclear tendency (13 pts.), no progression was found and 2 pts. showed regression with disappearance of anaplastic cells. This group of pts., however, had a tendency towards spontaneous regressions. A slight progression toward malignancy was found in the case of the definite anaplastic premalignant or dyskaryotic type (dysplasia). E had no direct influence on precancerous cells. An increased cell proliferation seemed to occur with therapy related to the monthly cycle (10 mg/day, from day 5-25 of the cycle, for at least 3 mo.). Decreased cell exfoliation with slight signs of cellular degeneration and incomplete maturation seemed to occur with continuous therapy (10 mg/day for at least 40 days). Stimulation of cellular proliferation and exfoliation occurred also after discontinuation of treatment with E, probably due to the side effects upon the hormone system. Side effects, such as changes in circulation, tissue and cell edema, and changes in parametrial appearance are similar to phenomena observed during pregnancy. Five illustrative cases are presented. The authors emphasize the need of cytologic examinations during long-term therapy with progestational drugs.

- 64-1276 THE CARCINOGENIC ACTION OF SEVERAL NITROGEN ISOSTERES OF CARCINOGENIC PENTACYCLIC HYDROCARBONS. (Fr., Abstract) Lacassagne, A., N. P. Buu-Hoi, F. Zajdela and P. Mabilie. *Path. Biol. (Paris)* 12(11-12/13-14):759, 1964.

In general, the substitution of a benzene ring by a pyridine ring decreases the carcinogenic effect. This effect was found to persist in 2/4 cases and to be increased in a third case. On the other hand, a great number of nitrogen isosteres are known to exist for each polycyclic hydrocarbon. This leads one to expect a greater possible number of carcinogenic compounds than can be expected from a study of condensed aromatic hydrocarbons alone.

- 64-1277 EXPERIMENTAL STUDIES ON SYNCARCINOGENESIS. (Ger., Abstract) Schmäh, D. *Krebsarzt* 19(1):43, 1964.

In addition to the material presented in CRA 1(4):#666, 1963, the author mentioned that with simultaneous admin. of diethylnitrosamine and 4-dimethylaminostilbene or X-ray, additive carcinogenic effects were not found. Syncarcinogenesis is demonstrable only when the substances which act simultaneously or one after another have the same organotropic effect.

- 64-1278 CHLORNAPHAZINE AS A BLADDER CARCINOGEN. (E.) Thiede, T. (Dept. Med., Finsen Inst., Copenhagen, Denmark), E. Chievitz and B. C. Christensen. *Acta Med. Scand.* 175(6):721-725, 1964.

Of 61 pts. treated for polycythemia with chlornaphazin, 20 received a total dose greater than 100 g. Seven of these 20 developed tumors of the urinary bladder: 2 carcinomas, 3 solid carcinomas, and 2 papillomas. In the 3 women and 4 men (aged 54-71) tumors were detected either during therapy (4) or at the time when treatment was discontinued (3). All but one pt. had also been treated with p32, 1 had also had X-rays and 1 also nitrogen mustard. Prolonged therapy with this agent is contraindicated.

- 64-1279 EXPERIMENTAL STUDY OF BRAIN TUMOR. (Jap.) Kawai, S. (Dept. Path., Gunma Hosp. Coll. Med., Japan). *Kitakanto Igaku (Kitakanto Med. J.)* 13(2):75-92, 1963.

In a study of experimentally induced brain tumors, the author implanted 20-methylcholanthrene pellets (approx. 2 mg in wt., 2 mm in length) into the subcortical area, the cerebellum, or the meninges in a total of 344 mice (approx. 25 g; 171 C3H, 63 ddN, 60 C57BL, 25 CF-1, and 25 CFW strains). For studies in Wistar and Donryu rats, see CRA 1(11):#1917, 1964. Among 234 mice that survived longer than 94 days, 112 developed tumors: 39 had gliomas; 63, sarcoma; 8, mixtures of glioma and sarcoma; and 2, indeterminate tumors. Out of the 39 gliomas which developed in an av. period of 275 days, 22 were classified as glioblastoma (14 developed in the cerebrum and 8, in the cerebellum; 11 in C3H; 6 in C57BL; 3 in ddN; one each in CF-1 and CFW). The others included 6 each oligodendroglioma and astrocytoma; 3 ependymoma; and 2 mixed. The 63 sarcomas were considered either giant cell or polymorphic cell sarcomas (31 developed in the cerebrum and 14 in the cerebellum). Isologous transplantation of the mouse tumors was successful in 19/26 gliomas, 4/4 mixed tumors, 16/27 sarcomas and 1/1 meningioma. In rats, 5/10 gliomas were transplantable into the same strain. Histopathological studies of these tumors, the author stated, showed that these experimentally induced tumors differed from human tumors and showed unique characteristics, especially in mice. The experimentally induced gliomas were the result of transformation of normal glial cells into tumor cells, which the author considered an indication that human glioma may develop by the same mechanism.

- 64-1280 BASIC STUDY OF CARCINOGENESIS BY CHEMICAL SUBSTANCES. (Jap.) Narukazu, O. (Sasaki Res. Inst., Japan). *Fukushima Igaku Zasshi (Fukushima Med. J.)* 12(3):306-307, 1962.

Male Donryu rats (age 6 wk.) given 0.05% 3'-methyl-4-dimethylaminoazobenzene (3'-Me-DAB) for 4, 5 or 6 mo. developed hepatomas. Transplants from the principal hepatoma (PH) and from additional hepatoma foci (AH) inoc. i.p. into mice of the same strain, after 4, 5 and 6 mo., led to the development of hepatomas in 4/8, 6/12 and 13/16 (81%), resp., of rats treated with tissue from PH; in

8, 4/12 (33%) and 6/16 (38%), resp., of rats treated with AH tissue; in 5/16 (31%), 10/24 (42%) and 19/32 (59%), resp., in rats treated with PH + AH. The transplantability of 3'-Me-B-induced hepatomas to normal rats was found to be proportional to the amount of the tissue transplanted in donors and to the rapidity of hepatoma proliferation in donors. Following admin. of 3'-Me-DAB (dosage not specified), which was discontinued before the development of adenomatous hyperplasia in the liver, application of 2-methylcholanthrene (MC; no details) to the skin, or admin. of 4-dimethylaminostilbene (no details), produced hepatomas in rats. Cancer of the skin was observed in rats given 3'-Me-DAB (no details; no other details) 11 mo. after topical application of MC (8x) to the skin. It is concluded that a carcinogen, even in small doses, can produce the initial minimal irreversible changes in a tissue, which subsequently undergo malignant transformation following admin. of a second carcinogen, regardless of the length of the intervening period.

1281 BIOCHEMISTRY AND PATHOLOGIC MORPHOLOGY IN CARCINOGENESIS. COMMENT. (Jap.) Sasaki, H. (Sasaki Res. Inst., Japan) and Odajima. *Nippon Rinsho* (J. *Jap. Clin. Med.*) 11(1):2407-2408, 1963.

Total of 18 groups of rats was fed DAB (0.06%), dimethylnitrosamine (AB; 0.06%), 20-methylcholanthrene (MC; 0.0067%), 4-nitroquinoline-N-oxide (NQ; 0.01%), 1-(2',4'-dimethyl)-phenylazo-2-naphthol (FR-5; 0.074%), 1-(2',4'-dimethyl)-phenylazo-2-disodiumsulfo-2-naphthol (FR-101; 0.128%), β -naphthylamine (NA; 10 mg/day) alone or in combination. The following incidence of hepatomas for DAB was seen: DAB for 2 mo. and 5 mo., 0 and 13/13, resp.; DAB for 1 mo., then AB for 1 mo., 0/12; DAB for 2 mo., then NQ for 3 mo., 0/12; DAB for 2 mo., then AB for 3 mo., 2/7; DAB for 2 mo., then MC for 3 mo., 3/7; DAB for 2 mo., then NA for 3 mo., 1/9; DAB for 2 mo., then FR-5 for 3 mo., 3/9; DAB for 2 mo., then FR-101 for 3 mo., 4/10. All the other combinations such as DAB for 4 mo., then DAB for 1 mo. caused no hepatomas in groups of 8-17 rats; FR-5 and FR-101 were ineffective. The results indicate that some carcinogens that are not strong alone induce hepatomas when admin. after a carcinogen such as DAB.

1282 CARCINOMA OF THE NASAL CAVITY IN MICE, FOLLOWING TOPICAL APPLICATION OF DIETHYLNITROSAMINE TO THE SKIN OF THE BACK. (Ger.) Mann, F. (Inst. Exptl. Cancer Res., German Cancer Res. Sci. Berlin) and A. Graffi. *Acta Biol. German.* 12(5):623-625, 1964.

2 drops of diethylnitrosamine (0.2% in acetone) were applied to the shaved backs of 4-week-old Agnes Bluhm and CBA mice of both sexes, for approx. 10 mo. (total dose, approx.

7 mg or 350 mg/kg), 17/24 animals which could be evaluated developed squamous cell carcinomas of the nasal cavity despite the absence of cancerous or precancerous changes at the treatment site. Carcinoma distribution was not influenced by sex or strain nor by additional treatment with croton oil (0.5% in acetone, 1-2 drops/dose, 1x/wk.) applied to the same treatment site. The authors question whether a specific organotropic effect was involved, or whether the animals inhaled the carcinogen immediately after treatment, thus bringing it into direct contact with the nasal epithelium.

64-1283 COMPARATIVE HISTOCHEMICAL STUDIES ON THE ACTIVITY OF SOME PHOSPHATASES IN TRANSPLANTABLE TUMORS AND THEIR HOMOLOGOUS NORMAL TISSUES. (Ger.) Butschak, G. *Acta Biol. Med. German.* 11(1):118-133, 1963.

Histochemical studies were made of various mouse tumor tissues (Ehrlich's carcinoma, Sarcoma S-37, Sarcoma Sala, 2 carcinomas induced by DMBA and a DMBA-induced sarcoma), rat tumor tissues (hepatic carcinoma induced by dimethylaminoazobenzene, Walker carcinoma, Yoshida carcinoma, Jensen sarcoma and a sarcoma induced by polyoma virus [PV]) and hamster tumor tissues (sarcomas induced by benzpyrene and PV). Compared to non-cancerous, homologous tissue samples, alkaline phosphatase activity was heightened in hepatic carcinomas, slightly increased in cutaneous carcinomas and extremely variable in the sarcomas. Acid phosphatase activity when determined by the metallic salt method was greatly increased in most tumor tissues; when determined by the azo dye method, it was significantly increased only in R-312 PV tumors and DMBA-induced carcinomas. Glucose-6-phosphatase activity was absent in all tumor tissues. Glucose-1-phosphatase activity was moderate in PV tumors of the hamster and weak in mouse Sarcoma S-37; hexose diphosphatase activity was also moderate in PV tumors of the hamster; no such activity could be demonstrated in any other tumor tissue.

64-1284 INFLUENCE OF MUTAGENS ON THE INITIATION OF SKIN CARCINOGENESIS. (E.) Trainin, N. (Dept. Exptl. Biol., Weizmann Inst. Sci., Rehovoth, Israel), A. M. Kaye and I. Berenblum. *Biochem. Pharmacol.* 13(2):263-268, 1964.

Male and female non-inbred Swiss/NIH mice (2.5-3.5 mo.; 21-38/agent) were admin. single i.p. inj. of urethan (U; 20 mg/mouse), acridine yellow (AY; 50 μ g/g), acridine orange (AO; 45 μ g/g), thymidine (T; 20 μ moles/mouse), 5-bromo-2'-deoxyuridine (BUDR; 20 μ moles/mouse), 5-iodo-2'-deoxyuridine (IUDR; 20 μ moles/mouse), adenine (A; 30 μ moles/mouse), 2-aminopurine (2-AP; 40 μ moles/mouse) or 2,6-diaminopurine (DP; 30 μ moles/mouse). Ten female inbred SWR/Jax mice received a single i.p. inj. of H^3 -thymidine (H^3 -T; 1.0 μ C/g). Four days after the inj., croton oil

(5% soln. in paraffin) was applied to the backs of all the mice, except those in the H³-T group, twice weekly for 20 wk., after which the animals were sacrificed. Incidence of lung adenomas was (agent and percent of mice): U 87, AY 18, AO 20, T 20, BUDR 17, IUDR 12, A 6, 2-AP 9, DP 17, H³-T 14; controls developed 8% adenomas. Skin papillomas (6) developed only in the U group. It was concluded that except for U, none of the agents significantly increases spontaneous lung adenoma in these animals nor do they induce skin tumors.

64-1285 POSSIBLE TERATOGENIC EFFECT OF CHLORAMBUCIL ON A HUMAN FETUS. (E.)

Shotton, D. (Lynchburg Gen. Hosp., Va.) and I. W. Monie. Transfusion 3(5):74-75, 1963.

A 30-year-old woman suffering from Hodgkin's disease became pregnant while being treated with chlorambucil; hysterotomy was performed at 4.5 mo. Although the fetus appeared normal externally, dissection revealed the absence of both the left kidney and ureter. This case is of interest because of the fact that when chlorambucil was admin. to pregnant rats on day 10 of gestation, a high incidence of unilateral or bilateral absence of the kidney and ureter was seen.

64-1286 STUDIES OF BUTTER YELLOW-INDUCED LIVER DAMAGE AND PROCESSES OF SPONTANEOUS RECOVERY. (Jap.) Akagi, Y. (Dept. Path., Kurume U. Sch. Med., Japan). Kurume Igakukai Zasshi (J. Kurume Med. Assn.) 26(10):772, 1963.

A more extensive presentation of the paper abstracted as CRA 2(5):#895, 1964.

64-1287 THE ROLE OF HORMONE AND VIRUS IN MOUSE BREAST CANCER. III. THE RELATIONSHIP BETWEEN HORMONES AND PRECANCER. (Jap., Abstract) Nishizuka, Y. (Dept. Path., Mie Pref. U. Sch. Med., Japan) and T. Sakakura. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Japon.) 52:234-235, 1963.

Estradiol (E) and progesterone (PR) were admin. to 7-8-week-old C3H/HeMs and Strain 129 female mice subjected to partial oophorectomy (OOX.) and/or simultaneous transplantation of isologous pituitary of males (for mammotropin, MH). The formation of hyperplastic alveolar nodules (HAN) in the breast varied significantly among the various strains of mice. OOX., admin. of E and/or transplantation of pituitary were done separately or concurrently in 8-month-old C3H, A/Jax and 129 mice which had had 2 or 3 pregnancies. OOX. caused disappearance of HAN in 60% of the mice and atrophy of HAN in the remaining mice, but some mice developed carcinomas. E combined with OOX. caused regeneration of HAN to 150% of normal. OOX. combined with transplantation of the pituitary caused a decrease in the number of HAN but cancer developed in many of the remaining HAN.

E and transplantation of the pituitary in the normal mouse resulted in hypertrophy of HAN (5 x normal) and the development of cancer in many cases. The results suggest that the formation and maintenance of HAN require E, PR and MH while the growth of HAN and probably carcinogenic changes require MH. When E was admin. for 4 mo. to (A/Jax x AKR)F₁ and (C3H x 129)F₁ mice (1.5-2 mo.), 52.6% of the former developed carcinomas 11 mo. after cessation of admin. of the hormone whereas 90.9% of the latter group had carcinomas 2.6 mo. after stopping the drug.

64-1288 A VISCOMETRIC STUDY OF HYDROGEN-BONDING PROPERTIES OF CARCINOGENIC NITROSAMINES AND RELATED COMPOUNDS. (E.) Argus, M. F. (Dept. Med. (Biochem.), Tulane U., New Orleans, La.), J. C. Arcos, A. Alam and J. H. Mathison. J. Med. Chem. 7(4):460-465, 1964.

In a viscometric study, dimethylnitrosamine and dioxane in mixtures with either water or propionic acid show large increases in viscosity above the values of ideal mixing; no such increase was seen in the absence of a proton donor, as in mixtures with benzene. Hydrogen bonding with propionic acid approx. parallels carcinogenic activity of a small series of nitrosamines (NT) and dioxane. The carboxyl group of proteins appears to be the main participant in the H-bonding of NT during protein denaturation by these compounds. Hydrogen bonding with NT is through the nitroso oxygen and involves displacement of the amino electron doublet, resulting in lack of basicity of the amino nitrogen. Aryl substituents decrease H-bonding by redirecting the displacement of the doublet.

64-1289 MULTIPLE TUMORS IN FEMALE GERMFREE INBRED ALBINO MICE EXPOSED TO BEDDING TREATED WITH ETHYLENE OXIDE. (E.) Reyniers, J. A. (Germfree Life Res. Ctr., Tampa, Fla.), M. R. Sacksteder and L. L. Ashburn. J. Nat. Cancer Inst. 32(5):1045-1057, 1964.

In germfree inbred female albino mice (ALBM-2, colony 101-GF) who survived 150-day exposure to ground corncob bedding sterilized with ethylene oxide, gross and microscopic examination revealed an 86.3% tumor incidence in 300-900-day-old animals. A wide variety of tumors were observed, including malignant lymphomas, pulmonary tumors, s.c. sarcomas, leiomyomas of the uterus, osteogenic sarcomas, tumor of the hardy gland, granulosa cell tumors and adenomas of the ovary, endometrial carcinomas and mammary tumors. Multiple tumors were observed in single animals. The most frequent tumors, in decreasing order of frequency, were ovarian, malignant lymphomas and pulmonary. Tumors occurred in females who were 10-577 days old at the time of exposure to the toxic bedding. Among 1 female and 2 males born 17 days before the bedding was changed, 1 male was found to have a pulmonary tumor. When bedded on untreated corncobs for up to 600 days ALBM-2

ice showed excellent reproduction and no tumors in males or females.

4-1290 DIFFERENCES IN SEX RATIO ACCORDING TO CANCER SITE AND POSSIBLE RELATIONSHIP WITH USE OF TOBACCO AND ALCOHOL. REVIEW OF 5,000 CASES. (E.) Flamant, R. (Gustave-Roussy Inst., Villejuif/Seine, France), O. Lasserre, Lazar, J. Leguerinais, P. Denoix and Schwartz. J. Nat. Cancer Inst. 32(6): 109-1316, 1964.

In a study of 65,000 cases of cancer where data on histology and site were available, the male/female sex ratio was very high for those sites with a very strong association with the use of both tobacco (T) and alcohol (A): hypopharynx, 28.0; larynx 27.4. Where the association with T was very strong and that with A strong, sex ratios were: oropharynx, 11.6; oral cavity (sites other than tongue and lips), 8.6. Where the reverse relationship held, sex ratios were: esophagus, 1.6; tongue, 9.3. With lung where a strong relation to T only was noted, sex ratio was 11.8. Where a strong relation to T only was noted sex ratio for lips was 8.1, for bladder and other urinary organs, 2.6. While no relation to A and was seen with the stomach, the sex ratio for the cardiac portion was clearly higher than for other regions of the stomach.

64-1291 STUDIES ON THE ASCITIC FORM OF LYMPHOCYTIC LEUKEMIA IN DBA MICE. (Jap.) O. M. (Dept. Int. Med., Okayama U. Sch. Med., Japan), K. Okada and N. Kawamura. Nippon Ketsueki kai Zasshi (Acta Hemat. Jap.) 26(3,4):391-392, 1963.

A new ascitic form of leukemia was produced in mice by inoc. of slices of lymph nodes obtained from DBA mice bearing 20-methylcholanthrene-induced lymphatic leukemia. This ascitic leukemia, designated OHO-LL, No. 1, has been successfully transplanted through 300 generations. The rate of success of transplantation, using 5×10^7 or 10^8 cells i.p. or s.c., was 100% in the same strain of mice. The av. survival time of the leukemic mice was 7 days. This form of leukemia is transplantable to Cba and R III mice (i.p. s.c.) and to 2b mice (i.p. only), but not to Strong A, D 103, C57 Black, or C58 Black mice. It was still transplantable after incub. at 7° or 20°C for 3 days, at 4°C for 1 wk., at 0°C for 3 wk., or -30°C for 9 wk. but failed to grow when transplanted after incub. at 56°C for 30 min. The frozen and dried ascites fluid could be transplanted when inoc. into newborn mice of the same strain.

64-1292 CARCINOGENIC ACTIVITY OF 4-(ISONICOTINYL-HYDRAZONE)PIMELIC ACID (4-INIP) IN MOUSE BALB/c/Cb/Se SUBSTRAIN. (It.) Milia, U. T. Cancer Res., U. Perugia, Italy), M. Gaetani

and C. Biancifiori. Lav. Ist. Anat. Univ. Perugia 24(1):39-47, 1964.

Following the intragastric admin. of 4-INIP (2 mg/day \times 150), 64 lung tumors developed in 37/51 (70.2%) female virgin 8-week-old BALB/c/Cb/Se mice. The induction time was 32 wk. The majority of the mice died between weeks 70 and 89. At autopsy, mice surviving the longest showed multiple pulmonary tumors (av. 1.73/mouse). Histologically, of 64 lung tumors, 55 (86%) were adenomas, 5 (8%) anaplastic adenomas and 4 (6%) carcinomas; one of the carcinomas metastasized to the paratracheal lymph nodes. Leukemia developed in 15/51 mice (29.4%); 14 also had pulmonary tumors, while one presented only leukemia. Differences between these results and those previously obtained with isonicotinic acid hydrazide and hydrazine sulfate (see CRA 1(9-10):#1698 and #1699, 1964) were explained as the result of a slower metabolism of 4-INIP by the organism.

64-1293 ATTEMPTS TO FIND CELL ASSOCIATED IMMUNE REACTION AGAINST AUTOCHTHONOUS TUMORS. (E.) Yoshida, T. O. (Inst. Infect. Dis., U. Tokyo, Japan) and C. M. Southam. Jap. J. Exp. Med. 33(6):369-383, 1963.

Spleen cells from C57 bl/6 black mice bearing tumors induced by 20-methylcholanthrene or 1,2,5,6-dibenzanthracene tended to inhibit the growth of transplanted tumor cells from the same mouse, as measured by growth of tumor + spleen cell mixtures on auto- and isotransplantation. Controls were mixtures of tumor cells with spleen cells from normal isologous mice. In 24-hr. tissue cultures, a specific adherence of spleen cells from some of the tumor-bearing mice to their autologous tumor cells was seen, while there was seldom such adherence to tumor cells in control preparations using spleen cells from normal isologous mice. In tests using the tanned erythrocyte agglutination technic, serum from a few tumor-bearing mice gave weak reactions with autologous tumor antigens. It is suggested that an autochthonous tumor encounters some degree of adverse host reaction.

64-1294 A LIGHT AND ELECTRON MICROSCOPE STUDY OF THE MORPHOLOGICAL CHANGES INDUCED IN RAT LIVER CELLS BY THE AZO DYE 2-ME-DAB. (E.) Lafontaine, J.G. (Dept. Path., Laval U. Sch. Med., Quebec, Canada) and C. Allard. J. Cell Biol. 22(1):143-172, 1963.

Light and electron microscope studies of hepatic tissue in Wistar rats fed 0.06% 2-Me-DAB for periods up to 16 wk. showed the following non-specific effects: disorganization of the arrangement of cisternal profiles of the granular reticulum; frequent irregular and fragmented appearance of the dispersed cisternae; presence of large cytoplasmic inclusions, consisting of loosely organized tubules and vesicles, which result from

agranular reticulum hypertrophy; progressive decrease in glycogen content. Many of these effects were similar to those seen with a potent carcinogen, e.g., 3'-Me-DAB. The most specific effect of 2-Me-DAB in cells was an increase in the number of mitochondria; these were characterized by the presence of a median double membrane continuous with the inner limiting membrane of the mitochondrial envelope. An increasing number of cells were also seen which stain intensely with methylene blue, appear denser than normal and are of unknown significance.

- 64-1295 THE REPLICATION TIME AND PATTERN OF HEPATOMA CELLS. (E., Abstract)
Hoffman, J. and J. Post. *J. Clin. Invest.* 43(6): 1269-1270, 1964.

The replication of rat hepatoma cells *in vivo* has been studied using the method of pulse-labeling of DNA and radioautography. Tumors were induced by 5 mo. of feeding 3'-methyl-4-dimethyl-aminoazobenzene, dissolved in corn oil, begun when rats were 3 wk. old. Animals were sacrificed 0.5-72 hr. after the admin. of labeled tritiated thymidine (H^3TDR), 1 $\mu C/g$ with specific activity of 0.36 C/mmole. The following time intervals were estimated: replication time, 31 hr.; DNA synthesis, 17 hr.; G_2 + mitosis, 2 hr.; G_1 , 12 hr. Approx. 8% of the tumor cell interphase population is flash labeled after a single inj. of H^3TDR . The tumor cell population in successive divisions differed from that of cells in normal rats in that the replication time is slower and there is more variation from cell to cell. It is concluded that hepatoma cell replication is under control and is not chaotic.

- 64-1296 DETERMINATION OF CONCENTRATION OF A CARCINOGENIC HYDROCARBON IN ANIMAL TISSUE BY GAS-LIQUID CHROMATOGRAPHY. (E.)
Gammal, E. B. (Dept. Med. Res., U. Western Ontario, Canada), K. K. Carroll and E. R. Plunkett. *Proc. Canad. Fed. Biol. Soc.* 7:5, 1964.

The procedure is described for the quantitative determination by gas-liquid chromatography of the conc. of 9,10-dimethyl-1,2-benzanthracene (DMBA) in the mammary tissue of female Sprague-Dawley rats following intragastric admin. at various intervals of DMBA in sesame oil.

- 64-1297 EFFECTS OF NEW LOW-DOSAGE FORM OF NORETHYNODREL-MESTRANOL. CLINICAL EVALUATION AND ENDOMETRIAL BIOPSY STUDY. (E.)
Flowers, C. E., Jr. (U. North Carolina Sch. Med., Chapel Hill). *J.A.M.A.* 188(13):1115-1120, 1964.

In 259 normal women given norethynodrel with mestranol (Enovid E; 2.5 mg and 0.1 mg p.o., resp.) through 3,510 menstrual cycles, there was no evidence that the oral progestin therapy caused an increase in the incidence of carcinoma of the

cervix; the drug did not change the chromatin pattern or the cytoplasmic-nuclear ratio of the cervical cells on the Papanicolaou smear. However, the author noted that some of the pts. had not entered the decades in which endometrial carcinoma is prevalent. The author states that there are no data to indicate that admin. of estrogen increases the incidence of breast cancer in humans.

- 64-1298 DIURNAL VARIATION IN THE SUSCEPTIBILITY OF MOUSE EPIDERMIS TO CARCINOGEN AND ITS RELATIONSHIP TO DNA SYNTHESIS. (E.) Frei, J. V. (Dept. Path., McGill U., Montreal, Canada) and A. C. Ritchie. *J. Nat. Cancer Inst.* 32(6): 1213-1220, 1964.

See CRA 1(8):#1473, 1963.

- 64-1299 THE ACTIVITY OF BLOOD LACTIC DEHYDROGENASE AND LIVER CATALASE IN MICE DURING CARCINOGENESIS. (Rus.) Mir'em, L. M. (P. A. Herzen Res. Inst. Oncol., Moscow) and A. P. Belousov. *Vop. Med. Khim.* 10(3):296-299, 1964.

In random bred C57 mice of both sexes undergoing carcinogenesis by o-aminazotoluol there was no significant change in lactic dehydrogenase activity (LDA) in the premalignant stage (60-130 days); with appearance of the tumor (3-5 mo.) LDA activity increased 2 to 2.5 times with subsequent return to normal levels at 6 mo. The activity of liver catalase in C57 mice increased during the premalignant stage; with the appearance of the tumors it decreased (in some animals there was a 6-7-fold decrease).

- 64-1300 ASSIMILATION OF AMINO ACID ANALOGUES BY A VIRUS-INDUCED TUMOR. (E.) Love, W. C. (Dept. Biol. Chem., Harvard Sch. Med., Boston, Mass.), A. S. Levine and J. Ashmore. *J. Nat. Cancer Inst.* 32(3):731-738, 1964.

Additional data are presented using the same experimental conditions as reported for CRA 1(4): #729, 1963. Concentration ratios (expressed as ratio of CPM/ml cell water:CPM/ml extracellular water) in Rous tumor slices and control chorioallantoic membrane (CAM) after 4 hr. incub. were 4.21 and 2.56, resp., for α -aminoisobutyric acid (AIB) and 3.71 and 2.85, resp., for l-amino-cyclopentane-1-carboxylic acid (ACC). Tumor tissue levels of AIB and ACC always exceeded the level observed in CAM; AIB accumulation in tumor slices continued to increase at a linear rate for periods up to 5 hr. Serine and valine (both 10 mM) markedly inhibited AIB and ACC conc. in tumor slices and in CAM. Both 2,4-dinitrophenol and anaerobiosis reduced AIB accumulation. Glucose (10 mM conc.) suppressed AIB accumulation in tumor slices, but had no effect on AIB accumulation in CAM.

64-1301 A TRANSPLANTABLE BERYLLIUM-INDUCED CHONDROSARCOMA OF RABBITS. (E.)

Higgins, G. M. (Texas Med. Ctr., Houston), B. M. Levy and B. L. Yollick. *J. Bone Joint Surg. (Am.)* 46-A(4):789-796, 1964.

A chondrosarcoma in the tibia of a rabbit, and its lung metastases, induced by the admin. of zinc beryllium silicate (5 ml of 1% suspension 2x/wk. x 10; total dose of beryllium stated as 3.3 g per animal), were successfully transplanted to the anterior chamber of the eyes of 6 rabbits. Tumor growth progressed in most rabbits; in 1/6 a graft surviving 7 mo. filled the anterior chamber and ulcerated through the cornea while in the other eye regression of the tumor after 2 wk. was seen; in 1/6 there was destruction of graft by infection in the left eye while the tumor grew in the right eye. The primary and metastatic tumors showed similar histology (undifferentiated and differentiated chondroblasts and chondrocytes with variation in staining intensity), while the transplanted tumor showed extreme pleomorphism of chondroblasts, multinucleated tumor giant cells and cartilage matrix in various stages of degeneration and calcification.

64-1302 AROMATIC-INDUCED PREVENTION OF FATAL TOXICITY OF 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.), E. Ford, R. Fukunishi and E. V. Jensen. *J. Exp. Med.* 119(6):943-954, 1964.

The inj. of large doses of 9,10-dimethyl-1,2-benzanthracene (DMBA; 20 mg i.v.) caused the death of 20 consecutive Sprague-Dawley rats in 16-21 hr. A small amount of 20-methylcholanthrene (MC), 3',6-DMBA, 4,5-DMBA, 1,2-benzanthracene or 6-aminochrysene, admin. before a toxic dose of DMBA (6 mg, i.v.) resulted in a survival of more than 2 mo. and the specific atrophy of the testis induced by DMBA was largely prevented. The inj. of a small dose of DMBA itself, when given prior to a toxic dose, induced protection in a proportion of the animals but did not impede testicular damage. The aromatic-induced protection required 5-8 hr. time for its effect. When ethionine was admin. prior to MC, the protective effect of the latter was abolished; when given 8 hr. after MC, no change in the protective effect was seen. The admin. of a lethal dose of DMBA caused considerable reduction in the incorporation of tritium in DNA from tritiated thymidine, while at the same time hepatic synthesis of menadione reductase was induced. A small dose of MC admin. prior to DMBA caused partial protection of DNA synthesis. (See also CRA 2(2):#222; and *ibid.*, (5):#890, 1964.)

64-1303 RIBONUCLEIC ACID METABOLISM IN LIVER NUCLEUS OF RAT FED CARCINOGENIC AMINO-AZO DYES. (E.) Kono, M. (Dept. Biophys., J. Tokyo, Japan). *Gann (Jap. J. Cancer Res.)* 55(3):251-257, 1964.

After the separation of nuclear RNA of rat liver into 3 different fractions (1. extraction of nuclei with 0.1 M phosphate; 2. treatment of sediment with 1 M NaCl; 3. remainder or residue), the RNA content and rate of orthophosphate (P^{32}) *in vivo* incorporation was determined during the feeding of dimethylaminoazobenzene (DAB; 0.06%) or 3'-methyl-DAB (0.062%) for 3-21 wk. The incorporation of P^{32} into the RNA of the residue fraction was stimulated approx. 2.8 fold at 10 wk., accompanied by a decrease in the amount of RNA. Little or no effect of DAB-feeding was observed in the other fractions. Guanylic acid content of residue RNA decreased markedly after 3'-methyl-DAB feeding for 8 wk., but the other fractions showed no change.

64-1304 AIR POLLUTION AND HEALTH. (E.)

Goldsmith, J. R. (California State Dept. Public Health, Berkeley). *Science* 145(2):184-186, 1964.

Succinct reports are presented from the 7th annual Air Pollution Medical Research Conference in Los Angeles, concerning pulmonary function and human exposure to cigarette smoke, peroxyacetyl nitrates, diluted diesel exhaust, ozone, sulfur dioxide and polluted air of cities (London, Los Angeles, New York City, New Orleans and Tokyo) and several other areas. Several studies of animal exposure to these products are also discussed. Mueller's *in vitro* study of the effects of gas and particulate matter in automobile exhaust on tissue cell cultures showed that the growth-stimulating property appeared to be associated primarily with the particle phase and was independent of changes from UV irradiation. Crocker, using organ cultures obtained from the trachea of suckling rats, showed that such carcinogenic hydrocarbons as 9,10-dimethyl-1,2-benzanthracene, 3,4-benzpyrene and 20-methylcholanthrene affected cell multiplication in the following way: DNA synthesis in basal cells increased before columnar cells changed form, metaplastic epithelium replacement of differentiated epithelium was characteristic for each product and, upon withdrawal of the hydrocarbon, differentiated cells reappeared while basal cell hyperplasia persisted.

64-1305 HISTOCHEMISTRY OF HYDROLYTIC AND OXIDATIVE ENZYMES IN EXPERIMENTAL SKIN CARCINOMA OF THE MOUSE. (E.) Auerbach, W. M. (Jewish Chronic Dis. Hosp., Brooklyn, N. Y.). *Cancer Res.* 24(6):937-945, 1964.

After interscapular application of 9,10-dimethyl-1,2-benzanthracene (0.03% 2x/wk. for 8 wk.) histochemical study of squamous hyperplasia and the induced carcinoma of the skin showed decreases in activity of acid phosphatase (AcPase), adenosine triphosphatase (ATPase), diphosphopyridine nucleotide (DPN) diaphorase and triphosphopyridine nucleotide (TPN) diaphorase when compared with normal mouse (Swiss albino) epidermis. DPNd and

TPNd were localized in the mitochondria in all cases, ATPase only in the hyperplastic and carcinogenic epidermis. Mitochondria in hyperplastic and cancerous epidermis were irregular in size and distribution and usually decreased in number compared to normal epidermis; AcPase activity was limited to the granular layers and cornified areas.

- 64-1306 THE SYNTHESIS OF 4,5-DIMETHYL-1,2-BENZ-ANTHRACENE AND 4,5,10-TRIMETHYL-1,2-BENZ-ANTHRACENE. (E.) Newman, M. S. (Evans Chem. Lab., Ohio State U., Columbus) and S. Blum. *J. Med. Chem.* 7(4):466-468, 1964.

Since 10-methyl-1,2-benzanthracene is active as a carcinogen while 1,2-benzanthracene is not, it is suggested that a reaction takes place at the 10-position (7-position using benz(a)anthracene nomenclature). The compound 4,5-dimethyl-1,2-benzanthracene was synthesized and found carcinogenic by others in rats (sarcomas in 5/7); it is believed that the methyls in the adjacent *peri* positions could block the reaction at the 10-position by sterically hindering a deactivating process. Tests reported in rats showed 3'6-dimethyl-1,2-benzanthracene and 1',9-dimethyl-1,2-benzanthracene to lack carcinogenic activity. (See also CRA 2(5):#891, 1964.)

- 64-1307 THE FATTY ACID COMPOSITION OF THE STEROL-WAX ESTER AND MONO- AND DIGLYCERIDE FRACTIONS OF MOUSE EPIDERMIS UNDERGOING NORMAL AND ABNORMAL GROWTH CHANGES. (E.) Carruthers, C. (Roswell Park Mem. Inst., Buffalo, N. Y.) and A. Heining. *Cancer Res.* 24(6):1008-1011, 1964.

Sterol-wax ester, mono- and diglyceride fractions were determined from the total lipid fraction of normal Swiss mice epidermis 4, 12 and 22 days following plucking of hair from methylcholanthrene-treated epidermis (topical painting on alternate days for 6-8 wk.) and carcinogen-induced squamous cell carcinomas. The sterol-wax ester fraction of the carcinomas differed from the normal or hyperplastic epidermis (which were essentially the same), in that it contained more palmitic, stearic and linoleic acid and less arachidic, methyl 11-eicosanoic, heneicosanoic, isobehenic, behenic and erucic acids. Arachidonic acid represented 12% of the carcinoma fraction whereas it was low or absent in the other two types. The

mono- and diglyceride fraction from the carcinomas contained more stearic acid than the other two types. In this fraction a sexual difference was noted: following plucking, female epidermis had a low level of lignoceric acid.

- 64-1308 VASCULARIZATION OF TUMORS INDUCED EXPERIMENTALLY IN THE CHEEK POUCH OF THE GOLDEN HAMSTER. (Fr.) Delarue, J. (Lab. Pathol. Anat., U. Paris, Sorbonne), J. Mignot and Gaulet. *Bull. Assn. Franc. Cancer* 50(4):553-566, 1963.

Tumors of the cheek pouch were produced by 1. transplantation of a malignant melanoma (35 hamsters, 28 takes); 2. intradermal inj. of dimethylbenzanthracene (DMBA), 20 mg, 5 inj. in 1 mo. (43 hamsters); 3. implantation of paraffin pellets with 100 mg DMBA (43 hamsters); and 4. painting of the mucous membranes with a 0.5% oily DMBA soln. 3x/wk. (85 hamsters). Vascularization of the tumors was followed *in vivo* as well as by histologic examination. Development of the melanomas was accompanied by marked vascularization around the transplants and formation of pedicles consisting of greatly dilated blood vessels derived from the host's vascular system. Methods 2 and 3 resulted in formation of sarcomas which also were characterized by marked vascular dilatation. Method 4 produced epitheliomas which from the beginning showed considerable disorganization of the subepithelial capillary network. In all instances, the degree of vascular disorganization paralleled that of histologically ascertained malignancy of the tumors. (See also CRA 1(4):#677; and *ibid.*, (6):#1097, 1963.)

- 64-1309 INFLUENCE OF AGE ON THE DEVELOPMENT OF MALIGNANT LYMPHOMAS AND HEPATOMAS IN SWISS MICE TREATED WITH URETHAN (ETHYL CARBAMATE). (It.) De Benedictis, G. (Inst. Path. Anat., U. Bari, Italy), L. Chieco-Bianchi, G. Tridente and L. Fiore-Donati. *Boll. Soc. Ital. Sper.* 40(11):610-612, 1964.

In addition to the results for hepatoma described in the paper abstracted as CRA 2(2):#230, 1964, the authors report that in Swiss mice treated with urethan (1 mg/g s.c.) at the age of 1, 5, 20 and 40 days, malignant lymphomas developed in 15/62 (24%), 9/36 (25%), 6/52 (12%) and 2/63 (3%) of the animals; induction period was 21, 23, 37 and 29.34 wk., resp. Incidence of spontaneous lymphoma was 8%.

See also abstract nos.: 1228, 1233, 1234, 1238, 1242, 1245, 1246, 1251, 1320, 1328, 1368, 1385, 1405, 1419

VIRAL CARCINOGENESIS

- 64-1310 ANTIGENIC CONVERSION OF ESTABLISHED LEUKAEMIAS BY AN UNRELATED LEUKAEMOGENIC VIRUS. (E.) Stück, B. (Sloan-Kettering Inst. Cancer Res., New York), L. J. Old and E. A. Boyse. *Nature (London)* 202:1016-1018, 1964.
- Ascites leukemia cells BALB/c male Gross No. 2, C57BL EL4 and BALB/c male U15 transplanted into BALB/c mice infected with Rauscher virus acquired the Rauscher antigen as shown by the cells' cytotoxic sensitivity to Rauscher antiserum. Ascites leukemia K36 (AKR) and ascites sarcomas C3H BP8, BALB/c Meth. A, and A strain of Sal were insensitive (or relatively so) following similar handling. When tested with Rauscher antiserum, a R/EL4 line passed serially in C57BL/6 mice showed no decline in sensitivity for the first, fourth and sixth transplant generation. The above BALB/U15 cells were ascitic, had the TL antigen and the hosts had generalized Rauscher disease. Sensitivity of the converted cells might be interpreted as meaning that viral replication occurred in the tumor cells.
- 64-1311 THE ISOLATION OF RAUSCHER MURINE LEUKEMIA VIRUS BY MEANS OF A CESIUM CHLORIDE DENSITY GRADIENT. (Fr., Abstract) Photini Chenaille, J.-P. Levy, M. Boiron and J. Bernard. *Path. Biol. (Paris)* 12(11-12/13-14):758, 1964.
- The Rauscher murine leukemia virus was found to possess biologic and morphologic properties very similar to those of the various known murine leukemogenic viruses. After purification by means of a cesium chloride density gradient of a crude virus extract prepared by differential centrifugation of blood from leukemic mice, the density of the virus obtained was 1.18. Its biological properties were not altered.
- 64-1312 FAILURE TO PROPAGATE A LACTIC DEHYDROGENASE-ELEVATING AGENT FROM MICE TUMOURS IN MICE EMBRYO CULTURES. (E.) Georgii, A. (Dept. Path., U. Munich, Germany) and I. Lenz. *Nature (London)* 202:1228-1229, 1964.
- Adult host mice were inoc. with 1-21-day-old cultures of mouse embryo cells incub. with cell-free filtrate from mouse sarcoma Sa-1, and their blood sera were tested 4-36 days after inoc. to determine the presence of an agent (presumably viral) expected to increase serum lactic dehydrogenase (LDH) activity. The LDH agent was present in tissue culture for a max. of 14 days (and in cell-free medium or saline for a max. of 4 days), but a successful technic for propagating the agent *in vitro* was not developed. (See also *CRA* 1(2):#255, 1963; and *ibid.*, 2(3):#521, 1964.)
- 64-1313 HORMONAL ACTION IN PRODUCTION OF TUMOURS AND COMPRESSION WOOD BY AN APHID. (E.) Balch, R. E. (Canada Dept. Forestry, Fredericton, N. B.), J. Clark and J. M. Bonga. *Nature (London)* 202:721-722, 1964.
- When the balsam woolly aphid, *Adelges piceae*, injects saliva via its stylets into the cells of *Abies balsamea*, hypertrophy and hyperplasia of the cortical parenchyma then occur in the fir. Abnormal growth stops with removal of the insect, thus a viral agent is not implicated. Several similarities between the effects of *A. piceae* saliva and an auxin, indolyl-3-acetic acid, were seen. Insect saliva may contain growth-regulating substances, but it is considered more likely that saliva upsets normal growth substances of the tree by enzymatic or synergistic action, inasmuch as the response to saliva is more pronounced in vigorous trees.
- 64-1314 ANTIBODY RESPONSE OF MICE TO A LEUKAEMOGENIC VIRUS. (E.) Greenspan, I. (Dept. Hemat., Cook County Hosp., Chicago, Ill.), E. R. Brown and S. O. Schwartz. *Nature (London)* 202:916-917, 1964.
- Antibody response in young adult ICR mice inj. with S-63 leukemia virus (determined by the passive cutaneous anaphylaxis and microprecipitin tests; see *CRA* 1(5):#905, 1963) in the 80% of survivors became max. after the time of max. leukocytosis (6-7 wk.). In a test designed to determine whether the antibodies were protective, groups of newborn mice were given i.p. inj. of serum from convalescing animals on 3 consecutive days. When challenged at 4 days with S-63 virus, 4/39 of this group died compared to 15/15 given normal mouse serum and 20/21 given saline before challenge.
- 64-1315 HETEROTRANSPLANTATION OF ROUS SARCOMA AND ROUS SARCOMA VIRUS TO MAMMALS. (E.) Schmidt-Ruppin, K. H. *Oncologia (Basel)* 17(3-4):247-272, 1964.
- Oral admin. or inj. (i.p., i.m., s.c.) of freeze-dried Rous sarcoma material (FD) caused more tumors in mice than did the fresh Rous sarcoma material (FS). Mice (Rüdiger strain) and rats (Wistar) fed FD or FS (5 g/animal/day x 22) in mashed bread induced 5 tumors. When transplanted into chicks, 2/3 mouse tumors grew as typical Rous sarcoma (RS). Rats (10; males and females) fed yolk or albumin (18 ml/day x 20 in milk) from eggs of infected hens showed some pathological findings and 1 lung tumor. Both supernatants and sediments of RS from chicks were active; however, the 18,000 R supernatant was less active than that from 5,000 R and the other preparations. Activity of the virus was higher in the presence of cellular components. Nasal applications of 18,000 R supernatant to Groppel strain mice induced tumors but only in 2 mice of 20 pretreated with croton

oil inhalations. In Groppel mice (sexes were kept apart) given FD plus slow acting estrogen, androgen, progesterone, cortisone or ACTH, only progesterone appeared to be a co-carcinogen. After admin. of FD + progesterone to 80 female mice, local tumor growth was enhanced. FD (one inj.) in pregnant mice and rats produced inconclusive results: only one unusual tumor in a male. When RS-induced tumorous liver and ascites from a rat were transplanted into 15 chicks (i.p.) and to 25 rats (i.p., i.m.), 6 chicks and 21 rats died with typical RS; however, transplants from later passages did not take.

- 64-1316 INFLUENCE OF VARIOUS VIRUSES ON THE HETEROTRANSPLANTABILITY OF HUMAN CELLS. (E.) Kissling, R. E. (U. S. Public Health Serv., Atlanta, Ga.) and B. V. Addison. *J. Nat. Cancer Inst.* 32(5):981-999, 1964.

Human diploid cells grown in the hamster cheek pouch survived longer than uninfected cells after infection with any adenovirus used (1, 2, 3, 7, 12 and 16), vaccinia, REO-2 or cytomegalovirus. The degree of autonomy of these cells did not equal that of cells of known malignant origin. Some viruses examined, including SV40, did not influence cell survival under these conditions.

- 64-1317 IMMUNE REACTIONS TO A MURINE LEUKEMIA VIRUS. I. INDUCTION OF IMMUNITY TO INFECTION WITH VIRUS IN THE NATURAL HOST. (E.) Fink, M. A. (NCI, Bethesda) and F. J. Rauscher. *J. Nat. Cancer Inst.* 32(5):1075-1082, 1964.

A more detailed presentation of the paper abstracted as CRA 1(4):#725, 1963.

- 64-1318 INFLUENCE OF HOST FACTORS ON DEVELOPMENT AND TYPE OF LEUKEMIA INDUCED IN MICE BY GRAFFI VIRUS. (E.) Fiore-Donati, L. (Inst. Path. Anat. Histol., U. Bari, Italy) and L. Chieco-Bianchi. *J. Nat. Cancer Inst.* 32(5):1083-1107, 1964.

When cell-free extracts (CFE) of leukemic tissues containing the Graffi virus (GV) were serially transmitted (0.05 ml inj. s.c. into the back region) to newborn mice of the AKR, XVII, C57BL, DBA/2, C3Hf/Gs and Swiss strains, the leukemia incidence (lymphatic, stem-cell and myeloid) was approx. 90%, with latent periods (LP) ranging from 13-20 wk. In AKR mice, inoc. of virus caused lymphatic leukemia (median LP = 14 wk.) almost exclusively; CFE of AKR lymphatic leukemia induced a significant number of the myeloid forms in strains C57BL and DBA/2. In C3Hf/Gs and AKR mice inoc. with GV, splenectomy did not modify the incidence and type of leukemia, while 76% of C3Hf/Gs mice and 40% of AKR mice that had been thymectomized developed myeloid leukemia. In sham-operated controls, 8% of C3Hf/Gs and 3% of AKR mice developed similar lesions. It is

concluded that the type of neoplastic response induced by GV is significantly influenced by the environmental conditions of the recipient hosts.

- 64-1319 ELECTRON MICROSCOPIC AND BIOASSAY STUDIES ON A MURINE LEUKEMIA VIRUS (RAUSCHER). I. EFFECTS OF PHYSICOCHEMICAL TREATMENTS ON THE MORPHOLOGY AND BIOLOGICAL ACTIVITY OF THE VIRUS. (E.) Zeigel, R. F. (NCI, Bethesda) and F. J. Rauscher. *J. Nat. Cancer Inst.* 32(6):1277-1307, 1964.

When purified murine leukemia virus was subjected to various treatments (ether, ethanol, formalin, trypsin, Triton X-100, 10 freeze-thaw cycles, temperatures of -70°, 4°, 37° and 56°C, centrifugal force, pellet resuspension, lyophilization, and osmotic shock), those preparations with a large number of intact particles had higher infectivity than those in which the virus appeared to be damaged. The type and severity of different morphological alterations, particularly the loss of "tail-like" extensions, was correlated with decreased infectivity. Treatment with distilled water resulted in disrupted particles with apparent release of particulate structures whose size, shape, and periodicity suggested a viral nucleoid origin. It was concluded that this virus is morphologically labile. (See also CRA 1(1):#101, 1963.)

- 64-1320 INHIBITION BY 3-METHYLCHOLANTHRENE OF INTERFERON FORMATION IN RAT-EMBRYO CELLS INFECTED WITH SINDBIS VIRUS. (E.) De Maeyer, E. (Dept. Virol., U. Louvain, Belgium) and J. De Maeyer-Guignard. *J. Nat. Cancer Inst.* 32(6):1317-1331, 1964.

See CRA 1(6):#1145, 1963; and *ibid.*, 2(2):#252, 1964.

- 64-1321 ANTIGEN CHARACTERISTICS OF VIRUS-INDUCED, HEMATOLOGICALLY DIFFERENTIATED, MOUSE LEUKEMIAS. (Ger.) Horn, K.-H. (Inst. Exptl. Cancer Res., German Acad. Sci. Berlin), G. Pasternak and A. Graffi. *Acta Biol. Med. German.* 12(5):626-628, 1964.

Supplementing a study reported previously as CRA 1(12):#2122, 1964, inbred mice of the XVII/B1n, C57/BL/B1n, CBA/B1n and AKR/B1n strains were used in the following study. Homologous transplants by suspensions of leukemic spleen and lymph node tissue (0.2-0.3 ml s.c.) of primary leukemias of lymphatic, reticular cell, or mixed reticular cell and lymphatic type (these types originally induced by cell-free filtrates of myeloid leukemias) regressed spontaneously after a few days. Then isologous myeloid leukemias (L 112b myeloid leukemia, L 129/6d chloroleukemia, PL 1462 paramyeloblastic leukemia, and L 184/3a myeloid leukemia), 10^5 and 5×10^5 cells, were inj. s.c. 14 days after immunization with homologous transplants.

Those mice developing no local tumor nor generalized leukemia for 6 mo. were classified as resistant. The percentage of resistant pretreated animals ranged from 56-88, versus 22%-27% of the controls. No resistance was developed in either of 2 groups of control animals receiving similar inoc. of L 1942 (Gross virus-induced) leukemia developed in and passed through AKR mice, or test animals pretreated by s.c. homologous transplants of a virus-induced lymphatic leukemia and a virus-induced leukemia with mixed lymphatic and reticulum cell components. The authors conclude that pretreatment of mice with homologous transplants of lymphatic and reticulum cell leukemias results in marked immunity against isologous transplants of purely myeloid leukemias. The absence of cross reaction between the Gross virus-induced leukemia of AKR mice and the lymphatic and lymphatic reticulum cell leukemias employed in pretreatment of this test group confirmed that the Gross virus was essentially a different type.

64-1322 EFFECT OF THYMECTOMY ON TUMOR INDUCTION BY POLYOMA VIRUS AND POLYOMA-INDUCED TUMOR CELLS. (E., Abstract) Defendi, V. (Wistar Inst., Philadelphia, Pa.) and R. A. Roosa. *Fed. Proc.* 23(2)(Pt. 1):393, 1964.

Hamsters were thymectomized (TX) either within 24 hr. after birth or at 7 days and then were given 350 r total body irradiation after 2 wk.; controls were sham-operated littermates. Tumors appeared earlier and in higher numbers per animal in those inoc. with polyoma virus (PV) 1 day after TX. When inoc. with PV at 3-4 mo., tumors occurred in 85% after TX compared to 20% in controls. In TX hamsters tumors were multiple; in controls they occurred only at the site of inj. In TX C57BL mice inoc. with PV at 3-6 mo., 6/20 developed parotid tumors. C3H and C57BL mice immunized with PV showed almost complete abolition of resistance to inoc. of 10⁵ isologous PV-induced tumor cells. No treated groups showed significant decrease in serum titer against PV hemagglutinating activity. Thus TX enhanced PV tumorigenicity by lowering immunological reactivity to the PV-induced antigen(s), without decreasing serum viral antibodies.

64-1323 VIRUS-LIKE PARTICLES IN HUMAN LEUKEMIC PLASMA. (E.) Burger, C. L. (Oak Ridge Natl. Lab., Tenn.), W. W. Harris, N. G. Anderson, W. Bartlett and R. M. Kniseley. *Proc. Soc. Exp. Biol. Med.* 115(1):151-156, 1964.

Differential and zonal ultracentrifugation, followed by brief ether exposure or by isopycnic banding in CsCl, yielded 2 types of virus-like particles (R and Q) from the plasma of 8 pts. (both sexes; age 15-77 yr.) with chronic myeloid ML; 3) or lymphatic (LL; 2) leukemia and acute or subacute ML (2) or LL (1) upon electron microscopic examination. R resembled the Rauscher virus; the head diameter was 200-300 mμ and the

tail length varied widely. The Q particle was hexagonal; it had an envelope surrounding an electron-dense center and a short narrow tail; the head diameter was 140-180 mμ and the intact tail width was 20 mμ. All the leukemic plasmas contained both or one of these entities. In 18 controls no R particles were found, but in one control Q-like particles were observed. The density of the particles was the same in all instances. All pts. but one had received radiation or unspecified chemotherapy. Of 3 pts. with chronic ML, 2 who had received radiation and chemotherapy had a much higher incidence of particles than the third untreated pt. The possibility that radiation and chemotherapy in man may cause the release of virus particles by a mechanism analogous to that observed in lysogenic phage exposed to ionizing radiation or chemical mutagens should be considered; the decreased immunological response which follows radiation treatment may also play a role in the increased number of particles.

64-1324 STUDY OF THE INFECTIOUS AND TUMORIGENIC ACTIVITY OF SV40 VIRUS. (PRELIMINARY REPORT.) (Rus.) Vasil'eva, N. N. (L. A. Tarasevich Control Inst., Moscow), A. T. Kravchenko, V. I. Gavrilov, N. N. Dodonova, I. S. Levenbuk and F. M. Karnaeva. *Vop. Virus* 9(2):222-227, 1964.

Subcutaneous inoc. of newborn Syrian hamsters (H) with SV40 (Strain A-426, Rh-2) resulted in development of sarcoma in 8/15 inoc. with 10^{4.6} TCID₅₀ and in 1/20 inoc. with 10^{3.6} TCID₅₀ within 125-202 days after infection. One animal, sacrificed at day 45 after tumor detection, had pulmonary metastases. Inoc. of 1-8 mo. old H with 20% primary tumor suspension s.c., intracranially, i.p. or intrapleurally led to tumor formation at the inoc. site in 68/75. Cell suspension incub. at 37°C for 3-4 days, showed a monolayer of spindle cells with round elements. This culture fluid with tumor cells inoc. s.c. into H led to development of tumors which tended to become necrotic. In a series of alternate tumor transfers from H to tissue culture to H, it was shown that the transplanted tumors had faster and more pronounced infiltrating growth (often with metastases to lymph nodes and lungs) than the primary tumors. Both tumor types, as a rule, contained the virus which was capable of inducing typical vacuolization of green monkey renal cells and which could be neutralized by specific immune sera.

64-1325 OCCURRENCE OF VIRUS-INDUCED TUMOR (VII): HISTOLOGICAL DEVELOPMENT OF POLYOMA IN THE MOUSE. (Jap., Abstract) Shimpo, K. (Dept. Path., Sapporo Coll. Med., Japan), K. Nishida, I. Fukushima and H. Kinoshita. *Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Jap.)* 52:237-238, 1963.

Inoculation of SE polyoma virus (Strain 4 B 5-6) s.c. in 72 newborn Swiss mice caused parotid tumors

of epithelial origin in 21 mice, as well as smaller numbers of kidney, breast, lung and thymus tumors. Six mice developed growth anomalies (dwarfs) and 2 of these had tumors in kidney and lung. In trials with the tumors which had developed, the breast tumors were successfully transplanted through 4 generations and the kidney tumors through one generation; there was no histological change.

- 64-1326 LEUKEMIAS OF THE NEWBORN (A STUDY OF 4 CASES). (Fr.) Bernard, J. (Inst. Leukemia Res., Saint-Louis Hosp., Paris), F. Chavelet and C. Jacquillat. Nouv. Rev. Franc. Hemat. 4(1):125-140, 1964.

Among 4 cases (3 females and 1 male) described, 3 had leukemia at birth; in 1 it was diagnosed on day 3. Maternal health was satisfactory; no radiation exposure, chemotherapy or viral infection had occurred during pregnancy. The fathers were reported to have been normal at the time of conception.

- 64-1327 PASSAGE OF LEUKEMIC CELLS ACROSS THE PLACENTA. (E.) Rigby, P. G. (U. Nebraska Sch. Med., Omaha), T. A. Hanson and R. S. Smith. New Eng. J. Med. 271(3):124-127, 1964.

Five hr. prior to delivery of a normal infant, the blood of its leukemic mother (acute myeloid leukemia), who was previously treated with 6-mercaptopurine and prednisone, was labeled with quinacrine. Two hr. after delivery, labeled cells resembling the mother's immature mononuclear WBC were found in the cord blood and, rarely, in the infant's blood, indicating the passage of WBC from the leukemic mother into the fetal circulation.

- 64-1328 THE ROLE OF PITUITARY HORMONE IN INDUCTION OF VIRUS-INDUCED BREAST CANCER. (Jap., Abstract) Yokoji, K. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan). Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Jap.) 52:235-236, 1963.

Breast cancers were induced in a period of 13 mo. in 16/37 LAF₁ mice (2.5 mo.), which have a low incidence of spontaneous breast cancer, by inoc. with Bittner's mammary tumor agent (virus) combined with a transplant of an X-ray-induced mammo-somatotropic pituitary tumor (Furth) to provide continuous secretion of mammotropin. No evidence of breast cancer was found in 159 mice treated with estrogen + virus, virus alone, mammotropic tumor transplant + estrogen, mammotropic tumor transplant alone, or estrogen alone. Most of the breast cancers which developed were not dependent on mammotropin, but this seems to be an important factor in promoting the development of breast cancer.

- 64-1329 SUBMICROSCOPIC MORPHOLOGY OF AVIAN NEOPLASMS. VI. COMPARATIVE STUDIES ON ROUS SARCOMA, VISCERAL LYMPHOMATOSIS, ERYTHROBLASTOSIS, MYELOBLASTOSIS, AND NEPHROBLASTOMA. (E.) Dmochowski, L. (Sec. Virol., U. Texas M D. Anderson Hosp. Tumor Inst., Houston), C. E. Grey, F. Padgett, P. L. Langford and B. R. Burmester. Texas Rep. Biol. Med. 22(1):20-60, 1964.

Results of the present electron microscope study indicate that the mode and sites of virus replication are similar if not identical in the cells of Rous sarcoma (obtained from chickens inoc. with the Bryan strain of RSV) and in the neoplastic cells of spleen of chickens with visceral lymphomatosis (induced with RPL-12 lymphoid tumor), myeloblastosis (BA1-A strain), erythroblastosis (Strains RPL-12 and R) and nephroblastoma. In the foregoing neoplastic cells, cytoplasmic inclusions (viroplasts), viral matrix (viroplasm) and budding of plasma membrane are encountered with varying frequency, with highest frequency in the epithelial cells of nephroblastoma. Cytoplasmic inclusions (viroplasts) are more frequently encountered in the reticular cells and macrophages of the spleen of infected chickens than in neoplastic cells.

- 64-1330 ASSOCIATION OF MYXOVIRUS-LIKE PARTICLES WITH ACUTE LEUKAEMIA OF CHILDHOOD. (E.) Benyesh-Melnick, M. (Dept. Virol., Baylor U. Coll. Med., Houston, Texas), K. O. Smith and D. J. Fernbach. Nature (London) 202:1129-1130, 1964.

Electron examination of serum and plasma samples from leukemic children has revealed the presence of numerous myxovirus-like particles, 90-250 mμ in size and with well-defined limiting membranes, which differed from those of murine leukemia by absence of "tails". Plasma or serum samples stained with potassium phosphotungstate and examined at 4,800-5,000x gave the following results (particles/field): in leukemic children 19/24 (79%) positive, 1 questionable, 4 negative; in normal children 4/40 (10%) positive, 8 questionable, 28 negative; in normal adults 13/13 negative. The 4 positive control children were all <12 mo. old, while 23/24 of the leukemic children were 2-10 yr. old. None of the 14 healthy children in this age group were positive, and only 3 were scored as questionable. It appears that there is no morphologic difference between the type of particles seen in the positive samples regardless of whether they came from leukemic or normal children.

- 64-1331 COMPARATIVE BIOCHEMICAL STUDIES IN NORMAL AND ERYTHROBLASTOSIS VIRUS-INFECTED CHICKENS. (Hun.) Sajgó, M. and P. Kertai. Magy. Onkol. 1(8):24-28, 1964.

White Leghorn chickens infected with the Engleberth-Holm "R" type erythroblastosis virus showed significant increase in serum Mg (43%),

chloride (18%), P (70%), serum lactic acid (248%), total protein (15%), and NPN (258%); while blood sugar and cholesterol were reduced 47% and 26%, resp. The nucleic acid content of the liver was increased 72%, with an 81% increase in DNA. Also, aerobic glycolysis of liver, spleen and kidney were considerably increased.

- 64-1332 HISTOGENESIS OF THYMIC LYMPHOMA INDUCED BY A MURINE LEUKEMIA VIRUS (RICH). (E.) Siegler, R. (Lab. Cancer Res., Albert Einstein Med. Ctr., Philadelphia, Pa.), J. Geldner and M. A. Rich. Cancer Res. 24(3): 444-459, 1964.

Inoculation (i.p.) of a newly isolated murine leukemia virus (Rich) into female 4-6-week-old BALB/c mice induced unilateral thymic lymphoma by 50-83 days. The evolution of the tumor portrayed the following histogenic pattern: early, slight bilateral thymic lymphocyte depletion, followed by late unilateral thymic lymphocyte depletion, unilateral lymphoma *in situ* and finally, unilateral lymphoma. No cells from the opposite thymus were involved in the last three steps. Anemia and the presence of tumor cells in the peripheral blood stream, lymph nodes, bone marrow and spleen occurred only at a very late stage of this lymphoma.

- 64-1333 THE ACCELERATING EFFECT OF CELL-FREE LEUKEMIC TISSUE EXTRACTS ON THE DEVELOPMENT OF LYMPHOGENIC LEUKEMIA INDUCED BY X-RAYS IN C57 BLACK MICE. (Fr.) Lázníčka, M. (Inst. Hemat. Blood Transfus., Prague, Czech.) and R. Smetanová. Bull. Assn. Franc. Cancer 50(4):651-658, 1963.

The i.p. admin. of cell-free extracts (CFE) prepared from the lymphopoietic organs of a C57 black male mouse with LaVUFB leukemia to C57 male and female adult mice 7 wk. prior to the i.p. inoc. of leukemia LaVUFB shortened the survival time one day (from 9-11 to 8-10 days), as compared with control mice previously inj. with a pyrogen-free saline soln. or with CFE prepared from spleens of healthy mice. The CFE from leukemic mice, when inj. i.p. into newborn male and female C57 mice, increased the incidence of leukemia to 44% (incidence of spontaneous leukemia is never greater than 4% in this strain). These studies suggest, but do not necessarily confirm, a viral origin of leukemia.

- 64-1334 POLYOMA VIRUS AND MOUSE STRAIN SUSCEPTIBILITY. (E.) Jahkola, M. (State Serum Inst., Helsinki, Finland) and T. Vainio. Acta Path. Microbiol. Scand. 61(1):60-66, 1964.

In vivo mouse strain susceptibility studies were performed in newborn C57BL/6 and DBA/2 mice (as well as their F1 hybrids) inoc. with moderately potent polyoma virus (0.05 ml) prepared from mouse embryo fibroblast culture. DBA/2 mice showed a tumor incidence of 43% (which occurred chiefly from 3-5 mo.), a 33% incidence of multiple tumors, and 65% bilateral parotid tumors. C57BL/6 and F1 hybrids showed a tumor incidence of <10%. *In vitro* studies revealed no differences in the course of polyoma infection in embryonic fibroblast cultures for C57BL/6, DBA/2, H-Albany and AKR/Lwn mouse strains. The various mechanisms of hereditary resistance to viral oncogenesis are discussed. The data indicated that susceptibility or resistance to polyoma oncogenesis is dependent on one or several hereditary factors (in C57BL/6), that it may be reflected in the behavior of a few specialized cells and that in a resistant strain the target organs may reach their susceptible stage of development earlier than in other strains.

- 64-1335 A QUANTITATIVE CELL CULTURE ASSAY FOR YABA TUMOUR VIRUS. (E.) Yohn, D. S. (Roswell Mem. Inst., Buffalo, N. Y.), J. T. Grace, Jr. and V. A. Haendiges. Nature (London) 202:881-883, 1964.

In vitro studies on the susceptibility of a variety of cell cultures to Yaba virus infection revealed the following: no infection in primary bovine kidney or chick embryo cells but infection of secondary rhesus monkey kidney cells (RMK) with undiluted inoculum (titer $10^{3.5}/0.2$ ml); infection of both RMK and rhesus fibroblasts with titer $10^{6.5}/0.2$ ml; an infectivity assay system in BSC-1 cells (a continuous cercopithecus monkey kidney cell line) equally as sensitive as tumor induction in the monkey. The onset of cytopathic effects (CPE) in BSC-1 varied with the dose; infection appeared to spread from cell to cell. Secondary foci were seen to appear during wk. 5 and thereafter. Since all foci which appear by day 21 are primary, the development of a highly quantitative but simple and inexpensive *in vitro* infectivity assay is thus possible. (See also CRA 2(2):#276, 1964.)

See also abstract nos.: 1220, 1225, 1232, 1238, 1240, 1241, 1242, 1243, 1245, 1246, 1247, 1258, 1300

- 64-1336 EPITHELIOMAS OF THE DORSUM OF THE HAND. REPORT OF 25 OBSERVATIONS. (Fr.) Chardot, C. and J. M. Carolus. Ann. Med. Nancy 3:154-166, 1964.

Of 418 skin carcinomas treated surgically at the Anticancer Center in Nancy (1955 and 1962), 25 were carcinomas of the back of the hand (right, in 13/25; left 12/25). The av. age was: male pts. (16/25) 68.6 yr.; female pts. (9/25) 71.8 yr. In 13/25 the epithelioma had been preceded by a precancerous condition: hyperkeratotic lesions due to sunlight or senile keratoses in 7/13, lesions related to chronic irritation due to handling of abrasives in 1/13 (an optician), radiodermatitis after X-irradiation for Raynaud's disease in 1/13, and old scars from mechanical trauma or burns in 4/13. Two of the tumors were basocellular while all others were spinocellular.

- 64-1337 MEDICOSTATISTICAL INFORMATION FROM DENMARK FOR THE YEARS 1961 and 1962. (E.) Dreyer, K., E. Frandsen and H. Hamtoft. Danish Med. Bull. 11(3):98-104, 1964.

A medicostatistical survey conducted in Denmark for the years 1961-62 revealed that malignant neoplasms constitute 22% of all deaths and rank second to heart disease as the chief cause of death. In 1962, cancer of the lung was responsible for 964 deaths in males and 213 in females, as compared to 969 and 185, resp., in 1961. The rate/100,000 for cancer of the lung was 41.8 for males, 9.1 for females and 25.3 for both sexes in 1962, as compared to 25.0 for both sexes in 1961.

- 64-1338 LOW PREVALENCE OF A-ANTIGEN IN CHILDREN WITH ACUTE MYELOID LEUKAEMIA. (E.) Hewitt, D. (Dept. Social Med., Oxford U., England) and P. S. Spiers. Lancet 2:93-94, 1964.

In a nationwide survey of childhood cancer conducted between 1953 and 1960 in England and Wales, ABO blood distribution for Groups O + B and A + AB, resp., was as follows: 60.8% and 39.2% in 309 children with acute myeloid leukemia; 53.8% and 46.2% in 785 children with other types of leukemia and also in 780 children with malignant disease other than leukemia; and 54.4% and 45.6% for normal blood donors. Studies on A-antigen deficiency in children with acute myeloid leukemia show that 14-15% of genotypically A or AB subjects who develop myeloid leukemia in childhood have O or B phenotypes. In apparent disagreement with published reports on all adult leukemias, it is postulated that subjects of O genotype may have an intrinsically greater liability to develop acute myeloid leukemia than subjects of A genotype, with an O:A risk ratio of about 1:3.

- 64-1339 MORTALITY IN LONDON IN THE WINTER OF 1962-63. (E.) Scott, J. A. (Public Health Dept., London County Council), I. Taylor, A. T. Gore and C. W. Shaddick. Med. Officer (London) 111(23):327-330, 1964.

In a study in London of the effects of temperature and air pollution, an increase was seen in the number of total deaths during the smog period of 1962 and during the cold spell of 1963. Higher mortalities were seen among the aged in both periods. The highest absolute increases were seen in deaths from cardiovascular disease (mainly old people), followed by deaths from bronchitis and other respiratory causes in both smog and cold periods. No similar increases were seen for lung cancer and other cancer deaths.

- 64-1340 GEOGRAPHIC DISTRIBUTION OF GASTROINTESTINAL CANCER. (E.) Ong, H. (U. Texas Med. Br., Galveston) and M. Patterson. Texas J. Med. 60(6):500-510, 1964.

In the search for possible etiologic factors, the geographic distribution of g.i. cancer deaths was studied in each of the 254 counties in Texas from 1953 to 1957. The percentage distribution of g.i. cancer deaths in relation to the total deaths from all causes ranged from 0-28.5%; av. was 4.4%. A mortality rate greater than 8% was seen in Blanco, Crane, Hansford, La Salle, Loving (2/7) and Motley counties, while McCulloch and Camp counties had death rates of 5.8% and 7.3%, resp. No correlations were found in relation to age, ethnic and socioeconomic groups, dietary habits, urban-rural residence, geographic regions and nature of soil.

- 64-1341 CONGENITAL LEUKEMIA. (E.) Christie, R. W. (Beatrice D. Weeks Mem. Hosp., Lancaster, N. H.) and W. L. Bergwall. J. Indiana Med. Assn. 57(7):749-754, 1964.

The case is presented of a male infant born with myelogenous leukemia, whose survival (11 mo. and 2 days) is considered the longest on record for this disease with or without therapy. It is suggested that congenital leukemia is the result of an injury occurring to the embryo between wk. 6 and 9. The infant's mother suffered an upper respiratory viral infection approx. 53 days after conception. The mother had also been admin. a number of medications during or immediately after pregnancy.

- 64-1342 FAMILIAL CANCER OF THE COLON. (E.) Kluge, T. (Dept. Surg. B, Riks Hosp., Oslo, Norway). Acta Chir. Scand. 127(4):392-398, 1964.

Carcinoma of the colon is reported in 7 members of a family of 11 individuals in 4 successive

generations. All cases were discovered at a relatively young age (36-53 yr.). Cancer of the colon is suspected in 2 other members, one dead and the other under close observation. The observations suggest a hereditary disposition for primary cancer of the colon, but seem to exclude hereditary precancerous factors. Of the 7 pts., 5 had previous surgery and 5 belong to blood group 0.

64-1343 HEREDITARY RETINOBLASTOMA. (Fr.) Watillon, M. (Dept. Ophthal., Baviere Hosp., Liege, Belgium), R. Weekers, E. Mairiaux and M. Joachim. *Arch. Ophthal. (Paris)* 24(3): 279-283, 1964.

Five members of a family in 3 successive generations were affected with retinoblastoma. In the first generation, 1 male was afflicted with the disease, while 1 clinically normal female who was found to be a heterozygote transmitted the disease to her offspring. In the next generation, 1 male who at 4 yr. of age presented bilateral retinoblastoma was cured by radiotherapy, 1 male died before the age of 2 of bilateral retinal tumors, and 1 female presented a scar interpreted as a spontaneously cured retinoblastoma. In the third generation, 1 male had bilateral retinoblastoma at 10 mo. and a 7-year-old female presented a pigmented lesion suggestive of retinoblastoma in 1 eye.

64-1344 SOME REFLECTIONS ON CANCER IN TROPICAL REGIONS. (Fr.) Camain, R. (Pasteur Inst., Paris). *Med. Afr. Noire* 11(6):231-234, 1964.

In a review of the literature (21 references) and the author's personal experiences (see also *RA* 1(5):#993, 1963; and *ibid.*, 2(1):#127, 1964), the peculiarities of malignancies in the tropics are compared to those observed in temperate climates are discussed. While reliable comprehensive statistics are still lacking, it is obvious that certain types of neoplasms, such as primary liver carcinoma, carcinoma of the cervix, and ENT tumors are more frequent in the tropics whereas bronchopulmonary, gastric, leukemias and cutaneous carcinomas show a higher incidence in temperate regions. There is great variation, however, from one tropical region to another; the incidence of liver carcinoma with respect to other tumors, e.g., is 30-40% in certain Swahilian territories of East Africa but only 5-20% in the area bordering on the Bight of Benin and in the equatorial regions. Etiologically, this type of tumor has been linked alternately to bilharziasis, nutritional factors, a hypothetic virus, and, recently, to the toxin of *Aspergillus flavus*. If genetic factors (pigmentation) protect the population of tropical countries to some extent from skin cancer, environmental factors (such as going barefoot) are responsible for a peculiar distribution of epidermal cancer; carcinomas of the

lower extremities on the basis of tropical ulcers are relatively frequent, regardless of the intensity of skin pigmentation. Malignant melanomas also are found predominantly below the knee, mostly on the heel; according to the author's statistics, 72/105 melanomas observed during a 13-yr. span were located on the foot.

64-1345 CANCER AND TRAUMA. (Fr.) Fauvet, J. (Gustave-Roussy Inst., Villejuif/Seine, France) and J. Roujeau. *Rev. Prat.* 14(17): 2183-2207, 1964.

Among 25,262 cancer pts. studied from 1949 to 1959 in the Institute, a relationship to trauma was found in 283 (1.02%) cases. Lesions involved, total cases and male and female number, resp., were: cutaneous epitheliomas 96 (62 and 34); cutaneous melanomas 26 (15 and 11); osteogenic sarcomas 31 (18 and 13); sarcomas of the soft tissues 24 (14 and 10); cancers of the mouth and oropharyngeal region 52 (42 and 10); cancers of the breast 45 (all females); cancers of the testicle 9. The interval elapsed between trauma and cancer discovery was one yr. or less in 43/95 epitheliomas, 11/26 melanomas, 43/55 sarcomas, 13/52 cancers of the mouth and ororhynopharynx, 28/45 cancers of the breast, and 8/9 cancers of the testis; in all remaining cases the interval was longer than 1 yr. Traumatic factors most frequently involved were stings, bites, cuts, burns, shock with hematoma, scratches, war wounds for epitheliomas; injury of a preexisting nevus for melanomas; impact followed by hematoma for sarcomas; repeated mechanical irritation for cancer of the mouth and ororhynopharynx, shock with hematoma or rib fracture for mammary cancer; violent impact with hematocele for testicular cancer. The incidence of post-traumatic cancer with respect to the total number of cases presenting the same condition was 3.2% for epithelioma, 10% for melanoma, 7% for sarcoma, 2.6% for cancer of the mouth and oropharyngeal region and 1.1% for mammary cancer.

64-1346 UTERINE CARCINOMA ACCORDING TO STATISTICS OF THE C.P.D.C.T. OF PERUGIA. (It.) Severi, L. (Inst. Anat., U. Perugia, Italy). *Riv. Anat. Pat. Oncol.* 24(5):1041-1046, 1963.

Analysis of 38,601 biopsy specimens examined from 1942 to 1962 in the Consorzio Provinciale for the Diagnosis and Cure of Tumors of Perugia revealed 5,609 malignant tumors which involved the breast (1,081), uterus (966), stomach and duodenum (808), intestine (574), skin (512), nasopharyngeal and laryngeal area (487), lymph nodes (403), lip, tongue and oral cavities (307), kidney and bladder (241), bone and striated muscles (230). Of 966 uterine carcinomas, 639 involved the cervix and 327 the body. The av. age was 51.63 yr. (range 20-89 yr.) for carcinoma of the cervix uteri and 55.07 yr. (range 20-79 yr.) for carcinoma of the corpus uteri. The former occurred more frequently

in the 5th and 6th decades of life while the latter in the 6th. The author also mentions that spontaneous uterine cancer occurs very rarely in animals; uterine sarcomas were found in 10.7% of mice (CBA/Cb/Se x BALB/cf/CB/Se)F1 of his laboratory at the av. age of 1,122 days.

- 64-1347 MULTIPLE PRIMARY CANCERS. (Fr.)
Fauvet, J. (Gustave-Roussy Inst.,
Villejuif/Seine, France), A. Chavy and R. Piet.
Rev. Prat. 14(17):2149-2174, 1964.

Among 25,262 cancer pts. studied from 1949 to 1959 at the Institute, 477 (1.86%; 195 males, 282 females; age 18-80 yr.) were found to have multiple primary cancer, of which 438 were double, 32 triple, 4 quadruple, 2 quintuple and 1 double with leukemia. Breast cancer associations were as follows: bilateral 154/221 pts.; breast + other site 67/221 (including uterine cervix 20, skin 17, ovary 8, corpus uteri 6, bronchotracheal 5, intestine 5, lip 2); double 54/67; triple 12/67; quadruple 1/67. Uterine cervix cancer was double in 44/47 pts. (including breast 20, skin 8, corpus uteri 5, intestine 4) and triple in 3/47 (breast + corpus uteri + ovary). Lip cancer was double in 21/27 pts., triple in 2/27, quadruple in 3/27 and quintuple in 1/27; associations included skin 22, ear-nose-throat (ENT) 5, tongue 3 and breast 2 cases. Cancer of the tongue was double in 35/38 pts., triple in 2/38 and quadruple in 1/38; associations included 12 cases with ENT (except larynx), 6 esophagus, 5 larynx, 5 bronchi. Of 184 cases of ENT cancer (except tongue and larynx), 71 were double, 11 triple, 1 quadruple and 1 quintuple; associations with other ENT cancers included 5 mouth, 8 pharynx, and 6 oropharyngeal cavity; associations outside ENT sphere included esophagus 15, skin 14, tongue 11, larynx 11, bronchi 10, prostate and colon 4 each. Of 56 laryngeal cancers, 49 were double, 4 triple and 1 quadruple: associations included ENT 14, skin 12, esophagus 10, bronchi 10, tongue 5, intestine 4, lip 3. Tracheo-bronchial cancers were double in 33/39 and triple in 6/39 pts. and associations included buccal cavity 13, larynx 10, breast 5, prostate 2. Of 40 pts. with esophageal cancer, associations were seen with ENT in 15, larynx 10, tongue 6, g.i. 3, skin 2; triple association (esophagus + mouth + colon) was seen in 1/40 pts. In 14 pts. with stomach cancer, associations included 6 skin, 3 ENT and 2 each of uterus, ovary, larynx and intestine. Intestinal cancer associations included breast 5, 4 each of ENT, uterus and larynx, and bronchi 3. Of 84 pts. with multiple skin cancer, other sites included lip 22, breast 17, g.i. 14, ENT 14, larynx 12, corpus uteri 8 and bronchi 5. The authors believe, from a study of this material, that treated cancer pts. are more prone to develop a second cancer than untreated pts., but that such increase in frequency varies with the localization. Also discussed are various hereditary, hormonal, and external factors which may play a role in the pathogenesis of multiple cancers.

- 64-1348 THE INCIDENCE AND SIGNIFICANCE OF MULTIPLE PRIMARY MALIGNANT TUMORS. (E.)

Thoma, G. W. (U. Texas M. D. Anderson Hosp., Houston). *Am. J. Med. Sci.* 247(4):427-430, 1964.

In a study conducted from 1944-1962, 2346 necropsies were performed on pts. with histologically proven cancer, and 4.2% showed multiple primary neoplasms. This group consisted of 69 males (ages 36-83 yr.), 29 females (ages 40-97 yr.), and 1 child. Nearly half (42%) of these multiple carcinomas were occult. Time between appearance of tumors was as follows: <1 yr., 18 cases; 1-2 yr., 11; 2-5 yr., 10; >5 yr., 18. Among those in which the malignancies were clinically evident, the second tumor was the cause of death in 70%, and no evidence of the first tumor was found at necropsy in 71%. If the time between the 2 tumors was 2 yr. or more, the first tumor was the cause of death in only 22%; in pts. in which the multiple tumors became manifest in 2 yr., the first tumor was considered responsible for death in 36%. The 12 cases which had tumors involving the upper respiratory tract and lung or esophagus comprised 21% of the cases where both tumors were clinically significant. Triple malignancies were observed in 5 pts. The 99 carcinomas were found in combination with 69 other carcinomas, 12 lymphomas, 8 leukemias, 2 myelomas, and 8 sarcomas.

- 64-1349 COMMENTS ON THE REPORT OF R. POCHE, O. MITTMANN AND O. KNELLER: "STATISTICAL STUDIES ON BRONCHIAL CARCINOMA IN NORTH RHINE-WESTFALEN." (Ger.) Koller, S. (Inst. Med. Statistics, U. Mainz, Germany). *Zschr. Krebsforsch.* 66(2):187-192, 1964.

A criticism is presented of the methods of study used by Poche et al (see CRA 1(3):#528, 1963) in their evaluation of lung carcinoma in different German cities. There was a lack of uniformity of histologic findings. Because of the absence of questionnaires from control subjects, the role of etiologic factors was limited to a comparison of squamous cell carcinoma to the remaining bronchial carcinomas. The author feels the material is not suitable for drawing conclusions regarding bronchial carcinoma and hence the lack of significant difference in reference to cigarette smoking is of no statistical importance.

- 64-1350 A STUDY OF 81 CASES OF SQUAMOUS CARCINOMA OF THE BUCCAL AND GINGIVAL MUCOSA. (E.) Mehta, M. J. *Indian J. Surg.* 26(4):306-318, 1964.

In a study conducted in India of 81 pts. (60 male, 21 female; av. age 47 yr., range 25-70) with squamous carcinoma of the buccal and gingival mucosa, distribution was as follows: 58/81 buccal (30 cheek, 20 cheek + lower jaw, 3 cheek + upper jaw, 5 cheek + upper + lower jaw); 17/81 lower alveolar; 6/81 upper alveolar. Of the 58 buccal cancers, 34 were on the left side, 22 right and 2

lip. Of the 23 alveolar cancers, 12 were on the left, 8 right and 1 center. The most frequent etiologic factor (51/81 pts.) seemed to be the chewing of raw tobacco mixed with chunna and keeping it on the same side of the lesion. Pan was chewed by 11/81; leukoplakia was present in many; positive VDRL was seen in 19/81 pts.; syphilis occurred in 23%. The relationship of this type of cancer to dental sepsis and stomatitis is also considered.

64-1351 CARCINOMA STOMACH--AN ANALYSIS OF 400 CASES. (E.) Fenn, A. S., C. K. Job, H. S. Bhat and V. Cherian. Indian J. Surg. 26(4):327-330, 1964.

In 400 cases of stomach carcinoma (which represents 5.9% of all malignant disease) seen at a hospital in southern India in an 11-yr. period, the male:female ratio was 5.3:1. The age range was 17-83 yr., with the highest incidence being between 50-60 yr. One quarter of the pts. had anaplastic or mucin-producing adenocarcinoma and 164 pts. were inoperable. The most frequent tumor sites in 385 cases were as follows: pylorus 201, cardia 65, lesser curvature 32, anterior wall and esophagus 25 each, greater curvature 20, posterior wall 9, whole stomach 8. There was no significant predominance of stomach cancer in any particular socioeconomic class even though the incidence was rather low in the poorer group.

64-1352 APLASTIC VERSUS HYPERPLASTIC BLOOD DYSCRASIAS. (E.) Doan, C. A. (Dept. Med., Ohio State U. Coll. Med., Columbus). Postgrad. Med. 35(6):564-570, 1964.

In a review on bone marrow damage induced by a wide variety of environmental agents, the age distribution is given for 1514 leukemia pts. seen at Ohio State University Clinic between 1930-1954. The highest peak of incidence occurred in the first 5 yr. (chiefly age 2-4 yr.), comprising principally the acute lymphosarcoma or acute lymphocytic leukemia of childhood. Chronic leukemia rose, less sharply, to a peak in the 6th decade. The lowest incidence of all kinds of leukemia was in the early teen-age group. Some of the cancer chemotherapeutic agents used against leukemia or against polycythemia are among the drugs which may induce aplastic anemia, sometimes including a leukemic phase, as a severe side effect.

64-1353 BRONCHIAL CARCINOMA AND THORACIC TRAUMA. (Ger.) Schlögl, J. (Ministry Social Welfare, Vienna, Austria). Wien. Med. Wschr. 14(24):419-421, 1964.

After a detailed presentation of a pt. with bronchial carcinoma who received thoracoplasty because of a wound received during the war and who died with metastases 19 yr. after the trauma, the author concluded that neither blunt trauma

and contusion of the thorax without an injury of the pleura and lung nor healed puncture injuries and bullet wounds can be considered to cause bronchial carcinoma. Callus formation after hemothorax, after empyema, or after residual cavities due to empyema, severe changes due to rib resection, dense callus layers, compression of lung and marked contraction in half of the thorax should be considered as essential causes in bronchial carcinoma.

64-1354 DEPARTMENT OF HEALTH. ANNUAL STATISTICAL REPORT. NATALITY AND MORTALITY, 1963. (E.) Wilbar, C. L., Jr. and R. E. Dwork (Eds.). Publ. Health Statistics, Dept. Health, Commonwealth, Pa., 81 pp., 1963.

In this comprehensive report for the state of Pennsylvania as a whole and its constituent counties, mortality due to neoplasms is given for 1963, 1962 and 1961 with comparison in some table with 10-year figures (1910-1960). Included are tabulations according to age, sex and site. Deaths from neoplasms have ranked second to those from heart diseases since 1940. For 1963 both the number of deaths due to neoplasms and the rate/100,000 represented increases over the preceding yr. (20,316 and 177.8 for 1963; 20,003 and 175.8 for 1962).

64-1355 AGE-ADJUSTED AND AGE-SPECIFIC DEATH RATES FOR MALIGNANT NEOPLASMS, 1960. (E.) Public Health Serv. Publ. #1113. U. S. Govt. Print. Office, Washington, D. C., 113 pp., 1963.

A report of the age-specific and age-adjusted death rates by color and sex for deaths from malignant neoplasms for the year 1960 for each state and for the U. S. as a whole. Data are given for neoplasms of various organs, including the lymphatic and hematopoietic systems.

64-1356 A REVIEW OF 995 CASES OF PRIMARY CARCINOMA OF THE LUNG. (E.) Haber, R. W. (Prince Henry Hosp., Sydney, Australia). Med. J. Aust. 1(15):551-556, 1964.

A total of 995 consecutive cases of histologically proven primary carcinoma of the lung treated from 1950 to 1958 in four Sydney teaching hospitals are reviewed. The peak incidence (710/995) occurred in the 51-70-year age group, with the highest incidence in the sixth decade of life (369/710). The age at the time of diagnosis ranged in this series from 17 to 85 yr.; 9 pts. were <30 yr. old. Relative to sex, 88% of all tumors occurred in men; however, for men there was a statistically significant higher rate for only the squamous type carcinoma (93.3%). For the group as a whole, tumor types were anaplastic carcinoma 48%, squamous cell carcinoma 38% and adenocarcinoma 12%. In this series, 53.2% of the cancers originated in the right lung and 44% in the left; the upper lobe

of each lung gave rise to more lesions than did the lower lobe.

- 64-1357 LEUKEMIAS AND THEIR FORMS (FROM THE AUTOPSY MATERIAL OF LVOV MEDICAL INSTITUTE AND THE LVOV REGIONAL CLINIC BETWEEN 1896-1960). (Rus.) Lutsik, D. P. (Lvov State Med. Inst., USSR). *Klin. Med. (Moskva)* 42(5): 12-14, 1964.

Among 53,892 autopsies performed between 1896-1960 there was a total of 541 cases of leukemia; incidence in an early period, 1896-1900, was 10/4,142 autopsies whereas in 1951-1955 and 1956-1960 it was, resp., 77/2,868 and 103/2,617. Total tumors during the same 3 periods were, resp., 224, 486 and 449. Leukemia deaths from 1951-1960 constituted about 90% of those due to blood diseases. In the whole series there were 324 males and 217 females; most were age 21-30 although acute forms were found frequently up to age 30. Reticulosis with destructive tumor growth was found in 243/541 (Hodgkin's disease in 136; lymphosarcoma, 73; acute reticulosis, 32); hemocytoblastosis was found in 8. Myeloid leukemia was found more often (155 cases) than lymphatic (83 cases). During the last 15-year period, acute myeloid leukemia was most frequent (53 cases); Hodgkin's disease was found in 35 cases.

- 64-1358 BASAL-CELL CARCINOMAS AND SEBACEOUS GLANDS. (E.) Graham, P. G. (Dept. Surg., Barnes Hosp., St. Louis, Mo.) and M. H. McGavran. *Cancer* 17(6):803-806, 1964.

Of 3,171 basal cell carcinomas recorded over a 10-year period, over 85% were located above the neck region. Furthermore, when areas of the face were arbitrarily delimited, it was seen that the frequency of tumors/cm² was directly proportional to the frequency of sebaceous glands in that area. The frequency of sebaceous glands and tumors was greater in exposed, than in shielded skin.

- 64-1359 PALATAL LEUKOKERATOSIS SECONDARY TO CANDELA PA DEN. A GEOGRAPHIC-MEDICAL NOTE. (E.) Schoenfeld, S. (Lago Oil Transport Co., Ltd., Aruba, Netherlands Antilles) and P. C. Holzberger. *Arch. Derm. (Chicago)* 90(1):89-90, 1964.

The study of 21 women (34-81 yr. old) who, since their teens, have practiced *candela pa den*, i.e., smoking with the lit end of the cigarette in the mouth, revealed the induction of palatal leukokeratosis but no malignant changes. Biopsies, from 6 pts. showed hyperkeratosis and acanthosis of the stratified epithelium, moderate infiltration of the focal areas in the subepithelial stroma by lymphocytes and histiocytes. The comment is made that this leukokeratosis is much more extensive than the "stomatitis nicotina" of pipe smokers described by Forsey and Sullivan.

- 64-1360 A PRELIMINARY SURVEY OF MALIGNANT LESIONS OF THE SKIN IN IRAQ. (E.) Alousi, K. (Dept. Bact., U. Baghdad Coll. Med., Iraq), G. F. Rahim and A. H. Fawzi. *J. Fac. Med. Baghdad* 6(3): 95-99, 1964.

In a survey conducted in Iraq, of 459 skin biopsy specimens examined, 224 were malignant. Of these, 56.2% were basal cell carcinomas from 73 males and 53 females (55.5% were 55 yr. or older). The incidence of other skin malignancies was: squamous cell carcinoma 30% (51 males, 24 females; nearly 50% over 50 yr. of age); melanoma 4% (1 male, 8 females; 40-60 yr.; in 5 the lesion was on the foot); and skin adenocarcinoma 1.77%. Other frequent malignancies (cases/total biopsies) included: lymph node, 152/387; gynecological, 122/1724; larynx, 111/212; breast, 71/157; pharynx and nose, 65/170; intestine and rectum, 49/209; lungs and pleura, 29/109; thyroid gland, 20/195; and prostate, 10/140.

- 64-1361 METAPLASTIC TRANSFORMATION FROM CIRRHOSIS TO CARCINOMA OF THE LIVER. (Jap.) Miyaji, T. (Dept. Path., Osaka U. Sch. Med., Japan) and S. Imai. *Shindan To Chiryo (Diag. Ther. [Tokyo])* 51(8):74-87, 1963.

In a statistical survey conducted in Japan from 1946-55 to study the relationship of cirrhosis to carcinoma of the liver, autopsy findings were as follows: 398 pts. (275 male, 123 female) with cirrhosis (A); 250 pts. (178 male, 72 female) with hepatoma (B); 168 pts. (146 male, 22 female) with combined cirrhosis + hepatoma (C). Of 62,242 autopsies examined in a similar survey conducted from 1958-61, results were as follows: 1,115 pts. (794 male, 321 female) with A; 500 pts. (342 male, 158 female) with B; 416 pts. (350 male, 66 female) with C. Cirrhosis was observed in 40.4% of all hepatoma (B + C) pts.; hepatoma was present in 29.7% of all cirrhotic (A + C) pts. In Japan a higher incidence of hepatoma alone and of cirrhosis in association with hepatoma was seen as compared to other countries.

- 64-1362 CANCER RATES AND RISKS. (E.) Bailar, J. C. III (Demography Sect., Biometry Br., NCI, Bethesda, Md.), H. King and M. J. Mason. *Public Health Serv. Publ. #1148*. U.S. Govt. Printing Office, Washington, D. C.

After reviewing the validity of the various indexes used in measuring the extent of illness due to cancer, the authors consider the incidence of and mortality due to cancer in relation to age, sex, type and site of cancer, geographic location, heredity, economic status, social customs and living habits, occupations, and environmental factors such as air pollution and radiation.

- 64-1363 END RESULTS IN CANCER. REPORT NO. 2. (E.) Clinical Biometry Section (NCI,

Bethesda, Md.). Public Health Serv. Publ. #1149. U.S. Govt. Printing Office, Washington, D. C.

In this work devoted to the evaluation of cancer therapy, a review is presented of the incidence of cancer by site of neoplasm as reported by more than 100 hospitals in the United States. The data are given for five-year periods between 1940 and 1959 or, in some cases, only for the period 1950-54.

64-1364 LEUKAEMIA OUTBREAKS? (E.) Heath, C. W., Jr. (Boston City Hosp., Mass.) and M. D. Manning. Lancet 1:1394, 1964.

In 4 areas of the U. S., during various periods between 1956 to 1961, the expected and observed number of cases (per 100,000) of leukemia was, resp.: Waldwick, N. J., 0.3 and 4; Cheyenne, Wyoming, 0.6 and 4; Chicago, Illinois, 0.4 and 4; Louisville, Illinois, 0.1 and 2. While the number of cases exceeded expectations by roughly a ten-fold margin, these figures are not statistically meaningful; the interpretation of such cases remains uncertain.

64-1365 STATISTICAL OBSERVATIONS OF MALIGNANT TUMORS OF THE SKIN. (Jap.) Yoshida, Y. (Dept. Derm., Tohoku U. Sch. Med., Japan), H. Onuma and H. Akiba. Rinsho Hifu Hinyokika (Derm. Urol. Clin. [Tokyo]) 18(1):59-62, 1964.

Among 21,124 dermatological outpatients seen during 1958-62, 44 cases (0.21%) of malignant tumors of the skin were observed. The male:female sex ratio was 13:12 for cancer, 10:2 for sarcoma and 2:5 for metastatic cancer of the skin. Age ranged from 2 mo. to 78 yr., and 77.3% were over 41 yr. old. Relatively lower incidences of skin tumors were seen among outpatients for the periods 1928-37 (0.07%) and 1938-42 (0.15%). Skin cancers developed from burn scars (4), xeroderma pigmentosum (4), X-ray irradiation (2), lupus vulgaris (1) and unknown origin (14). The most frequent site (60%) was the face. As for histology, 14 were spindle cell carcinomas, of which 6 developed on the face and 4 from unknown origin; 10 were basal cell carcinomas, of which 8 developed on the face and 9 from unknown origin. Metastatic skin cancers, histologically identical with their primary sites, developed from the breast (3), rectum (1), uterus (1), prostate (1) and unknown site (1). The skin sarcomas found were derived from leukemia (5), reticuloendothelioma (6) and Kaposi's sarcoma (1).

64-1366 MORTALITY DUE TO MALIGNANT NEOPLASMS IN POLAND DURING THE YEAR 1959. (Pol.) Staszewski, J. (Inst. Oncol., Gliwice, Poland). Nowotwory 14(1):63-78, 1964.

Neoplasms comprise the second most frequent cause of death in Poland (about 10% of total deaths,

i.e., 26,196 of 252, 430 dying in 1959), exceeded only by deaths due to circulatory diseases. In 1959, mortality (per 100,000 of population) due to neoplasms was highest in the city of Poznan (152.69 men and 157.42 women) and lowest in the district of Szczecin (60.77 men and 58.60 women). Since, for a number of reasons, the above crude tabulations of mortality were considered unreliable, they were broken down to urban versus rural areas. In urban areas, mortality (per 100,000 of population) due to various malignancies in men was: esophagus, 4.18; stomach, 30.7; larynx, 11.03; respiratory tract, 18.63; leukemia, 10.65; and other lymphatic and hematopoietic malignancies, 4.57. Similarly mortality rates for urban women were: stomach, 22.4; other areas of digestive tract, 21.1; respiratory tract, 4.78; breast, 8.94; uterine cervix, 5.3; uterine body, 13.06; ovaries and adnexa, 5.53; various metastases with unknown primary, 11.51; and undefined malignancies, 5.65. Death rates of remaining tumor locations were less than 4/100,000.

64-1367 CANCER MORTALITY IN THE COMMUNITY OF BRESCIA FROM 1901 to 1960. (It.) Tarantini, F. (Dept. Health Sanit., Brescia, Italy) and G. Dossena. Ann. Sanit. Pubblica 25(1): 93-99, 1964.

Cancer mortality (per 10,000 people) in Brescia [Lombardy] was 12.2 in 1901-1905, 13.2 in 1911-1915, 11.1 in 1921-1925, 11.9 in 1931-1935, 12.9 in 1941-1945, 15.6 in 1946-1950, 18.8 in 1951-1955 and 19.5 in 1956-1960. Analysis of the cancer distribution by site showed that the incidence of tumors of the g.i. tract, breast, genitourinary system and oropharynx, with respect to other localizations, did not vary from 1901 to 1960, while a gradual increase was seen for tumors of the respiratory system (2.6% in 1901 and 12.7% in 1960) and for those of lymphatic and hematopoietic systems (0% in 1901 and 5.77% in 1960).

64-1368 SMOKING IN RELATION TO MORTALITY AND MORBIDITY. FINDINGS IN FIRST THIRTY-FOUR MONTHS OF FOLLOW-UP IN A PROSPECTIVE STUDY STARTED IN 1959. (E.) Hammond, E. C. (Am. Cancer Soc., New York). J. Nat. Cancer Inst. 32(5): 1161-1188, 1964.

This survey is based on questionnaires answered by 422,094 men (age 40-89 yr.) followed for an av. of 34.3 mo. Death rates (deaths due to all causes) were markedly higher among cigarette smokers than in nonsmokers, and higher in those who started cigarette smoking at a young age than in those starting at a later age and in current cigarette smokers than in ex-cigarette smokers who had quit for 1 yr. or longer. For cancer as a whole (all sites combined), the mortality ratio of cigarette smokers to nonsmokers was 1.98 for the age range 40-69 yr. and 1.75 for the age range 70-89 yr. Mortality ratios were also high, resp.,

for cancer of the lung (7.86 and 19.07), buccal cavity and pharynx (5.54 and 2.33), esophagus (3.67 and 8.32), bladder (3.31 and 3.16), and pancreas (2.95 and 1.90, resp.). Considerably higher death rates (deaths due to all causes) were seen in men who smoked 20 or more cigarettes/day than in nonsmokers, in all subgroups studied, including grouping in terms of parental longevity, history of cancer in parents or siblings, race, religion, education, marital status, etc. Among 36,975 matched pairs of subjects, 1,385 cigarette smokers as compared to 654 nonsmokers died; 110 smokers died from lung cancer as compared to 12 nonsmokers. The proportion of men hospitalized for all causes during the first 2 yr. of study was considerably higher among cigarette smokers than among nonsmokers and increased with the amount of cigarette smoking and degree of inhalation. (See also CRA 2(2): #181, 1964.)

64-1369 SMOKING AND LUNG CANCER. (Ger.)

Auerbach, O. (Dept. Path., New York Coll. Med., N. Y.), A. P. Stout, E. C. Hammond and L. Garfinkel. *Fortschr. Med.* 82(11):405-408, 1964.

In an autopsy study of the tracheobronchial systems of 63 male pts. dying of lung cancer and 339 dying of other causes, no precancerous changes or carcinomas *in situ* were found among 65 nonsmokers included in the latter group. Among the remaining subjects dying of causes other than lung cancer, precancerous changes increased in direct proportion to the reported daily consumption of cigarettes. In the light of additional material derived from 11 hospitals in northern New York State (a total of 1522 cases), the authors conclude that more cells with atypical nuclei were found among male cigarette smokers than among female cigarette smokers; that no significant differences were seen as between urban and rural, all female nonsmokers or female nonsmokers in 2 age groups separated by 30 yr.; that comparable age groups of male cigarette smokers showed a significant increase of cells with atypical nuclei among the older group; and that nonsmoking males showed significantly fewer epithelial changes or cells with atypical nuclei. (See also the following abstract.)

64-1370 SMOKING HABITS AND AGE IN RELATION TO PULMONARY CHANGES. RUPTURE OF ALVEOLAR SEPTUMS, FIBROSIS AND THICKENING OF WALLS OF SMALL ARTERIES AND ARTERIOLES. (E.) Auerbach, O. (Dept. Path., New York Coll. Med., N. Y.), A. P. Stout, E. C. Hammond and L. Garfinkel. *New Eng. J. Med.* 269(20):1045-1054, 1963.

In a study of lung sections from 1340 men who came to autopsy (at the VA Hospital in East Orange, N. J., from 1955 through 1960) it was found that rupturing of the alveolar septums, fibrosis or thickening of the alveolar septums,

thickening of the walls of the arterioles, thickening of the walls of small arteries and pad-like attachments to the alveolar septums were found significantly more frequently among men who had smoked 1-2 packs of cigarettes per day than among those who had been nonsmokers, and among older as contrasted to younger cigarette smokers. The immediate cause of death was lung cancer in 172/1340 pts. studied (including 166 cigarette smokers, 5 pipe or cigar smokers, 1 nonsmoker); cancer of other sites in 442/1340. (See also the preceding abstract.)

64-1371 RADIATION, CHROMOSOMES AND VIRUSES IN THE ETIOLOGY OF LEUKEMIA. EVIDENCE FROM EPIDEMIOLOGIC RESEARCH. (E.) Miller, R. W. (NCI, Bethesda). *New Eng. J. Med.* 271(1):30-36, 1964.

In an extensive review of the etiology of leukemia, the author presents experimental and clinical data on radiation-induced leukemia, including the leukemogenic effects of atomic bombing in Hiroshima and Nagasaki, partial-body exposures for radiation therapy and intrauterine exposure to diagnostic radiation. Chromosome abnormalities as causative or predisposing factors in leukemia, as seen in the concurrence of mongolism (see CRA 1(2):#286, 1963), miscarriages and leukemia, are also discussed. Although viruses have been shown to be oncogenic in laboratory animals, to induce malignant transformation in cultures of human tissue, to provoke numerous chromosomal aberrations and to interact with the leukemogenic effects of radiation, epidemiological research has not proven the viral origin of human leukemia.

64-1372 THE ROLE OF EPIDEMIOLOGY IN THE ETIOLOGY OF LEUKEMIA. (E.) Miller, R. W. (NCI, Bethesda). *CA* 14(4):130-134, 1964.

A brief presentation of the paper presented in the preceding abstract; see also CRA 2(4):#800, 1964.

64-1373 CONTRIBUTION TO THE INCIDENCE OF MALIGNANT TUMORS IN TWINS. (Cz.) Herold, J. (Dept. Oncol., Charles U. Sch. Med., Prague, Czech.), J. Venta and M. Zavadil. *Cas. Lek. Cesk.* 103(14):361-366, 1964.

There is reported the cases of a monozygotic pair of females (age 34 yr.) with simultaneous occurrence of carcinoma of the uterine cervix. Hereditary predisposition is discussed. A review of the literature (7 references) on correlation in incidence of various diseases, including tumors, in homozygous and heterozygous twins is presented.

64-1374 PRESENT STATUS OF LEUKEMIA IN JAPAN WITH SPECIAL REFERENCE TO EPIDEMIOLOGY AND STUDIES ON THE EFFECT OF CHEMOTHERAPY. (E.)

Wakisaka, G. (Dept. Int. Med., Kyoto U. Sch. Med., Japan), H. Uchino, T. Nakamura, S. Shirakawa, A. Adachi, M. Sakurai and K. Miyamoto. Acta Haemat. (Basel) 31(4):214-224, 1964.

The annual death rate from leukemia in Japan rose from 0.51/100,000 of population in 1910 to 1.3 in 1940, 1.5 in 1950, and 2.8 in 1960. Leukemia death rates for males were 1.26 to 1.56 times higher than those for females. Leukemia deaths per 10,000 from all causes rose from 2.4 in 1910 to 7.8 in 1940, 13.5 in 1950, and 37.2 in 1960. However, the leukemia death rate/100,000 population is lower in Japan than in most other countries. Between 1956 and 1961 the incidence of acute leukemia in Japan was relatively higher than that in western countries, but incidence of chronic leukemia was lower. Total leukemia cases (3454) recorded in leading hospitals of Japan (1956-61) were distributed as follows: acute myeloid 56.8%, acute lymphatic 8.7%, acute undifferentiated 5.9%, chronic myeloid 19.2%, chronic lymphatic 2.6%, chronic basophilic and eosinophilic 0.1%, monocytic 6.7%.

64-1375 MORTALITY BY OCCUPATION AND CAUSE OF DEATH AMONG MEN 20 TO 64 YEARS OF AGE: UNITED STATES, 1950. (E.) Guralnick, L. (Mortality Statist. Br., U. S. Dept. Health, Educ., Welfare, Washington, D. C.). Vital Statistics (Spec. Rep.) 53(3):93-339, 1963.

This analysis based on deaths in 1950 of U. S. males (total, white and nonwhite) with work experience includes deaths from all neoplasms as well as by site in reference to ages 20-64 in 5 or 10-year cohorts; standardized mortality ratios are also presented. Included are all the occupations in the intermediate occupational classification (which is presented in detail).

64-1376 CANCER MORTALITY PATTERNS AMONG U. S. URANIUM MINERS AND MILLERS, 1950 THROUGH 1962. (E.) Wagoner, J. K. (NCI, Bethesda), V. E. Archer, B. E. Carroll, D. A. Holaday and P. A. Lawrence. J. Nat. Cancer Inst. 32(4):787-801, 1964.

Cancer mortality patterns of a group of U. S. uranium miners and millers were studied, and their age-race-cause-specific mortality experience was compared with that of the general male population of the Colorado Plateau area. Among white U millers, no significant difference was seen between the observed and expected total and cause-specific mortality; among white U miners, 218 deaths were observed, 148.7 were expected ($P < 0.01$). Categories in which observed deaths significantly exceeded that expected were: respiratory neoplasms (11 observed, 1.1 expected) and "all other causes" in miners with 5 or more yr. of underground experience. The increase in incidence of respiratory cancer was not attributable to age, smoking nativity, heredity, urbanization, self-selection, diagnostic accuracy,

or prior hard-rock mining or other ore constituents (including silica dust), but was correlated with airborne radiation. (See also CRA 1(7):#1359, 1963.)

64-1377 EARLY DIAGNOSIS OF GYNECOLOGIC CANCER WITH THE AID OF CYTOLOGY. (Ger.) Kern, G. (Women's Hosp., U. Cologne, Germany), E. Rissmann and G. Hund. Arch. Gynaek. 199(5):502-525, 1964.

The results of cytological examinations of 22,249 smears of the cervix and portio uteri among a study group of 13,674 pts. in a women's hospital were positive with respect to epithelial changes indicative of cancer in 4%, suspicious in 1.1%, negative in 80.7%. There was a significant difference in the mean age of pts. with suspicious or positive findings, 46.2, compared to that of pts. with negative findings, 42.1. There was no significant difference between the incidence of suspicious and positive findings among pre- and postmenopausal pts. The percentage incidence among women with 0, 1, 2, 3, 4 and 5 or more children was 3.1, 5.1, 5.4, 7.1, 8.3 and 12.1, resp. Histologic follow-up studies confirmed 615 benign cervical specimens, 174 early cases of cervical carcinoma (1.3% of the study group), 206 other cases of cervical carcinoma and 80 cases of carcinoma of the corpus uteri. The authors conclude that the incidence of cervical carcinoma increased progressively and significantly with the increase of reported childbirths. On the basis of statistical projections compensated for false negative cytological findings, they also conclude that the overall incidence of cervical carcinoma in situ is probably between 1.6-2.7%.

64-1378 LEUKEMIA IN CHILDREN AND YOUNG ADULTS IN NORWAY. TYPE DISTRIBUTION, INCIDENCE, AND SURVIVAL. (E.) Bjelke, E. (Sch. Public Health, U. Minnesota, Minneapolis). Cancer 17(2):248-255, 1964.

According to the Cancer Registry of Norway, 242 new cases of leukemia were diagnosed between 1953 and 1958 among the population under 20 yr. of age; this represents 30.5% of all cancer in this age group and an annual rate of 5.3/100,000. Leukemia was most common in children of the 2-4 yr. group. Incidence was similar for both sexes for ages 0-9 yr. but thereafter it was higher among males. Over 97% of all the cases were classified as acute leukemia and, where the leukemic cell type was specified (131 pts.), the ratio of myeloid:lymphatic leukemia was 5:1. The mean survival time was longer during 1956-58 than during the previous 3 yr. During the same period (1953-1958), 11.7% of the cancers in persons under age 20 were malignant lymphomas.

64-1379 MORBIDITY RATE, MORBIDITY AND MORTALITY OF LEUKEMIA IN POLAND DURING THE YEARS 1951-1959. PART II. MORBIDITY AND MORTALITY.

(Pol.) Janicki K. (3rd Clin. Int. Dis., Acad. Med. Sci., Cracow, Poland). *Pol. Tyg. Lek.* 19(27):1023-1025, 1964.

Leukemic morbidity rate (number of registered and hospitalized cases per 10,000 of population) in Poland during 1951-1959 was lowest (3.0-4.0) in the districts of Szczecin, Olsztyn, Lodz, Kielce, and Rzeszow; it was high (6.0-7.0) in the city of Warsaw, and highest (7.0-8.0) in the city of Lodz. Ecologic factors were suspected, but further studies are indicated. A steady, statistically significant increase in mortality due to leukemia during 1951-1959 was evident, whereas general mortality showed a decrease in 1951-1955, increased in 1955-1957, and decreased in 1957-1959. (See also CRA 1(9-10):#1775; *ibid.*, 2(2):#374; *ibid.*, (3):#548; *ibid.*, (6):#1169; and *ibid.*, (7):#1366, 1964.)

64-1380 A CANCER PRONE FAMILY. DISCUSSION OF THE QUESTION OF INHERITABILITY OF COLONIC CARCINOMA. (Ger.) Heinzelmann, F. (Dept. Surg., St. Clara Hosp., Basel, Switzerland). *Helv. Chir. Acta* 31(3):316-324, 1964.

A male pt. is presented who, at different times over a period of approx. 30 yr., developed 3 primary carcinomas of the colon. In 5 generations of the same family 13/85 members developed carcinomas (including a brother of the pt., who developed 2 primaries); 10/13 of these were colonic carcinomas (the remaining cases were 2 carcinomas of the uterus, 1 mammary carcinoma). In the 3rd generation of the family, to which the pt. belonged, 2/3 brothers had died of colonic carcinoma; 1/2 sisters died of a uterine carcinoma. One of 2 male nephews had died of colonic carcinoma, while another had been operated upon for the same disorder. None of the pt's. own 3 children were cancerous, up to the time of report. Both of the pt's. parents died of cancer of the large intestine, as did 1/2 of his paternal aunts and 1/2 of the affected aunt's children. The author concludes that this and other genealogic studies which have been reported seem to indicate that a hereditary predisposition to cancer is of decisive importance in actual carcinogenesis.

64-1381 MORTALITY IN GERIATRIC DISORDERS. CONDENSED MORTALITY TABLES AND THEIR IMPLICATIONS. (Ger.) Oehmisch, W. (Inst. Social Hygiene, Berlin-Lichtenberg, Germany). *Deutsch. Gesundh.* 19(23):1076-1082, 1964.

A comparison of E. German mortality statistics for 1960-61 with those for 1932-33 indicates that

the probability of a given individual's dying from cancer has increased only slightly for males in all age groups and has decreased slightly for females in all age groups above 45. The increased probability for males is attributed to the increase in lung cancer, deaths from other types of cancer having decreased considerably. Excluding the influence of age, cancer deaths in males have increased from 13-16% of deaths due to all causes, an insufficient amount to alter statistical probability significantly for a given individual at birth. Among females, cancer deaths have remained approx. constant (14.5-14.2% of deaths due to all causes), decreasing statistical probability significantly for a given individual at birth, in view of the uniformly decreased probability beyond age 45. The author comments that mortality data for W. Germany are essentially similar.

64-1382 FATAL ACCIDENTS IN CHILDHOOD AND YOUTH IN THE GERMAN DEMOCRATIC REPUBLIC IN THE YEAR 1962. (Ger.) Marcusson, H. (Inst. Social Hygiene, Berlin-Lichtenberg) and W. Oehmisch. *Deutsch. Gesundh.* 19(23):1038-1045, 1964.

In a review of accidental deaths among children and adolescents (ages 1-20) in East Germany, cancer deaths/10,000 persons of the same age groups are cited as 0.45 (males) and 0.37 (females) in 1933 (all Germany), 0.67 (males) and 0.63 (females) in 1953 and 0.82 (males) and 0.59 (females) in 1961. The corresponding percentages for the 3 yr. (taking deaths due to all causes as 100%) were 1.9, 5.5 and 8.2, resp., for males and 1.8, 7.1, and 9.2, resp., for females.

64-1383 THE SURGEON GENERAL'S MALIGNANT TUMOUR REGISTRY. (E.) Tooley, R. W. (Dept. Prev. Med., Surg. Gen. Staff, Ottawa, Ontario, Canada) and A. H. Sellers. *Med. Serv. J. Canada* 20(6):541-545, 1964.

Since its inception in 1960 to 1963 the Surgeon General's Malignant Tumour Registry showed a total of 314 (307 males, 7 females) new cases of cancer among Canadian service personnel; the overall crude incidence was 62.4/100,000 male strength, male age adjusted rate was 67.6 Army, 66.7 Navy and 51.2 Air Force. Percentage distribution, according to tumor site, was: skin 29.7; RES and g.i. 16.3 each; genitourinary 14.4; respiratory 12.1; brain and central nervous system 5.2; buccal cavity and pharynx 3.3; others 2.7. Large bowel cancers were found in 22 Army as compared to 10 Air Force personnel; bladder cancer in 10 Army as compared to 4 Air Force personnel. The age-specific rates increased sharply with age, except for the Air Force where the number of cases at age 50 is too small to be significant.

See also abstract nos.: 1236, 1237, 1241, 1275, 1290

MISCELLANEOUS

- 64-1384 CARCINOMA AND CONTAGION? (It.)
Macaggi, G. B. (Dept. Surg., Celestia
Hosp., Genoa, Italy). Rass. Arch. Chir. 2(1):
56-62, 1964.

The author describes briefly 94 cases of carcinoma, each of which had lived in close proximity with one or more subjects who also developed carcinoma either previously or subsequently within a period of time ranging from a few mo. up to 8 yr. The possibility of contagion between the various members of a family (up to 4 in some cases) is discussed since the relationship, in view of the high number of cases observed, appears to be more than casual.

- 64-1385 GENETIC CARRIER FREQUENCY FOR LUNG
CANCER. (E.) Burch, P. R. J. (Dept.
Med. Phys., U. Leeds, England). Nature (London)
202:711-712, 1964.

In a brief review of the literature (10 references) concerning genetic factors in transmission of leukemias and lung cancer, it was pointed out that an extrinsic carcinogen (associated with smoking) can induce pulmonary tumors in individuals not carrying the genetic factor. If approx. 50% of the lung cancers were prezygotic (i.e., due to a mutant arising in the germ cells as contrasted to postzygotic or arising in somatic cells) then the frequency of a predisposing allele in the population is likely to be much less than 3%. (See also CRA 1(3):#371, 1963.)

- 64-1386 THE GENETIC CODE OF MAMMALIAN CELLS.
(E., Abstract) Ochoa, M., Jr. and I. B.
Weinstein. J. Clin. Invest. 43(6):1247, 1964.

A group of synthetic messenger RNA's, differing in their content of adenylic (A), cytidylic (C), guanylic (G) and uridylic (U) acids, have been tested with seven C^{14} -amino acids in extracts of human chronic lymphocytic leukemia, mouse L1210 leukemia and normal rat liver cells. Results show that the minimal number of nucleotides necessary to code for each amino acid is as follows: for phenylalanine, U; for leucine, either U + G, U + A, U + C or U alone; for serine, U + C; for tyrosine, U + A; for isoleucine, U + A; for lysine, A; for valine, U + G. Similar results were obtained with other mammalian systems and with *E. coli*. Sucrose gradient fractionation of L1210 microsomes indicated that whereas native protein synthesis occurs predominantly on polyribosomes, both single ribosomes and polyribosomes can engage in protein synthesis directed by synthetic messenger RNA. Studies with fractionated microsomes indicated that polyadenylic acid, in addition to coding for lysine, appears to enhance the function of endogenous messenger RNA. It is concluded that malignant transformation of cells is not accompanied by major alterations in

the genetic code or in the over-all mechanism of protein synthesis.

- 64-1387 RAPIDLY PROGRESSIVE COURSE OF CANCER IN
THE LIGHT OF THE PATIENTS' "ANXIETY
SCALE." (Ger.) Herberger, W. (Hufeland Clin.,
Wittenberg, Germany). Zschr. Psychosom. Med.
9(4):271-285, 1963.

An intimate relationship was found to exist between the general psychological state of cancer pts. and the rate of development of their disease. In 12/15 case histories reported in detail, rapid progression of the disease was linked at least partially to severe psychological trauma resulting in depression and lack of desire to live; in 3/15, remarkable emotional stability and ability to cope with psychological stress were felt to be conducive to long survival. The pts. included 12 females, ranging in age from 33 to 74 yr., and 3 males, 51-53 yr. The malignancies in the female pts. included 8 mammary, 1 cervical, 1 ovarian and 1 pancreatic carcinoma, and 1 chronic myeloid leukemia; in the males there were 2 bronchial and 1 gastric carcinomas. Survival time ranged from 4 mo. to 2.75 yr. in the pts. with depressive tendencies, but was 4 yr. in the 3 pts. able to compensate their psychological conflicts.

- 64-1388 DEFICIENCY IN ERYTHROCYTIC H ANTIGEN IN
A LEUKEMIC PATIENT OF WEAK PHENOTYPE A.
(Fr.) Salmon, C. (Dept. Med., Saint-Antoine
Hosp., Paris), J. Debray and A. Lemaire. Nouv.
Rev. Franc. Hemat. 4(2):245-251, 1964.

In a 64-year-old female pt. with acute leukemia, immunological studies were performed prior to therapy and transfusions. The pt. presented a weak phenotype A. Agglutinability of RBC by anti-A was comparable to that of normal A_x erythrocytes; agglutinability by human and vegetable (*Ulex europaeus*) anti-H reagent, however, was between that of normal A₁ and A₂ erythrocytes. This incongruity indicates a deficiency in H antigen. It seems possible that the abnormalities observed in the ABH phenotypes involve 2 independent genes: the H-forming X, and the A-forming A gene. A study of the karyotypes of the pt. revealed 1 abnormal cell (partial deletion of a chromosome of group 13-15) among 26 examined.

- 64-1389 CHROMOSOME ABNORMALITIES IN A CASE OF
ACUTE LEUKEMIA WITH BONE MARROW APLASIA.
(It.) Pegoraro, L. (Inst. Clin. Med., U. Turin,
Italy), A. Pileri and F. Gavosto. Haematologica
(Pavia) 48(9):713-719, 1963.

In a 58-year-old man with bone marrow aplasia, cervical lymphadenopathy, and hepatic and splenic enlargement, chromosome preparations from marrow

cultures revealed the presence of a long sub-metacentric chromosome (similar to that found in the peripheral blood) in all mitoses, thus confirming a diagnosis of acute leukemia. Study of karyotypes showed that one chromosome of pair 1 was missing; the long chromosome was therefore assumed to be the result of the translocation of an extra chromosome in one of the two chromosomes of pair 1. This alteration was found in only 10% of mitoses from peripheral blood cultures of the pt. and was absent in cultures of blood from his father and brother, thus excluding the possibility of a congenital or hereditary abnormality.

- 64-1390 RECKLINGHAUSEN'S DISEASE IN THE INFANT. (Fr.) Roget, J. (Clin. Child., Grenoble, France), A. Beaudoin, Y. Gilbert and J. Marchioni. *Pediatric* 19(4):421-428, 1964.

Three siblings (2 males and 1 female), born 2-3 yr. apart, showed the typical symptoms of Recklinghausen's disease at birth; 2/3 had cutaneous and osseous lesions, 1/3 had cutaneous lesions and, probably, a laryngeal tumor. In the 2 older children, the manifestations disappeared completely, without treatment, at the age of 5 and 2.5 yr. The youngest child was only 5 mo. old when the report was written. The development of the children progressed satisfactorily. Twelve similar cases from the literature are reviewed (21 references); it is assumed the disease in the neonatal period is relatively benign and tends to regress spontaneously. A systematic investigation of the fate in adulthood of pts. affected by the disease in infancy is advocated.

- 64-1391 TRAUMA AND TUMORS OF THE TESTICLE. (It.) Ascoli, R. (Traumatolog. Ctr., I.N.A.I.L., Milan, Italy) and A. Fava. *Minerva Chir.* 19(8):289-292, 1964.

A 31-year-old man observed enlargement and hardening of the right testicle following impact; when removed 62 days later histologic examination showed growth to be an embryonal carcinoma. A seminoma was also found in the left testicle of two men (age 32-49 yr.), resp., 35 and 222 days after they had suffered trauma to the area. In these 2 cases the short interval involved suggested that the neoplasm was already present at the time of trauma, even if in a latent stage.

- 64-1392 CHROMOSOME NUMBER AND MORPHOLOGY OF A HUMAN PREINVASIVE NEOPLASM. (E.) Richart, R. M. (Dept. Path., Columbia U. Coll. Phys. Surg., New York) and P. A. Corfman. *Science* 144(1):65-67, 1964.

Cervical epithelium taken from 5 pts. with varying degrees of histologically proven cervical neoplasia (3 with dysplasia, 2 with carcinoma

in situ) was found to grow in tissue cultures using Eagle's minimal essential media with 15% fetal calf serum at 37°C, 5% CO₂ and air. After one or more (max. of 4) successive transfers, metaphase plates made from these cells revealed an essentially normal diploid chromosome distribution and a normal karyotype. The authors feel that abnormal chromosomes previously reported in cervical cancer cells came principally from the non-reproductive cells of this tumor.

- 64-1393 HEPATOMA CARCINOGENESIS AND ITS RELATION TO PATHOLOGICAL CHANGES OF REMAINING LIVER TISSUE. (E.) Saito, M. (Dept. Path., Fac. Med., U. Tokyo, Japan). *Acta Path. Japon.* 13(4):240-241, 1963.

After an examination of 114 cases of hepatomas in relation to different types of cirrhosis, the pathological findings suggest the possibility that hepatomas may arise from long-standing and relatively mild liver injury (toxins or nutritional disorder). Histological examination showed that small liver cells, adenomatous hyperplasia, adenoma formation and to some extent nodular hyperplasia are more frequently seen in liver in cases of hepatoma. Some abnormal karyotypes were found.

- 64-1394 MULTIPLE MYELOMA IN 2 SISTERS. AN IMMUNOCHEMICAL STUDY. (E.) Leoncini, D. L. (Hosp. Nacional Clinicas, Buenos Aires, Argentina) and L. Korngold. *Cancer* 17(6):733-737, 1964.

An immunochemical study was made of the urine and serum of 2 sisters (60 and 67 yr. old) with multiple myeloma. The serum of 1 pt. contained large amounts of gamma-1A-myeloma globulin (g-1A-M); the urine and serum were both negative for Bence Jones protein (BJP). The serum and urine of the second sister contained BJP, but there was no other abnormal serum globulin. However, antigenic typing showed that this BJP and the g-1A-M both belonged to group 2. A brief review of familial multiple myeloma is presented (14 references).

- 64-1395 MALIGNANT MELANOMAS IN SMALLPOX VACCINATION SCARS. REPORT OF SIX CASES. (E.) Marmelzat, W. L. (Dept. Med., U. So. California Sch. Med., Berkeley), P. Hirsch and S. Martel. *Arch. Derm. (Chicago)* 89(6):823-826, 1964.

Six cases (3 male: ages 33-76 yr. at time of diagnosis) of proven malignant melanoma occurring within a smallpox vaccination scar (5 deltoid, 1 thigh) are presented. In 3 cases the interval from vaccination was known (7, 7 and 50 yr.); in another case the lesion had been noted for 5 yr. when first diagnosed. Four additional cases of malignant melanoma of this same origin have been reported to the authors.

64-1396 CAN POLYCYTHEMIA VERA BE TRANSFORMED INTO CHRONIC MYELOID LEUKEMIA? (Ger.) Braunsteiner, H. (2nd Dept. Med., U. Vienna, Austria), G. Rothenbuchner and B. Schober. Med. Clin. 59(15):614-618, 1964.

The Philadelphia chromosome, which is characteristic for chronic myeloid leukemia, could not be found in any of the 13 pts. examined (9/13 with polycythemia vera (PV) and 4/13 with osteomyeloclerosis (O)). In the cases of PV and O which were eventually transformed into a picture clinically similar to chronic myeloid leukemia, a normal karyotype was found.

64-1397 DERMATOMYOSITIS AND BREAST CANCER. (Sp.) Mazzei, E. S. (Fac. Med., Buenos Aires, Argentina) and A. Delmar. Rev. Clin. Esp. 90(4):217-222, 1963.

Case histories are presented of 2 women (age 39 and 59 yr., resp.) showing the coexistence of dermatomyositis (DM) and breast cancer. Mastectomy and treatment of the neoplasm were found to benefit the DM. In a review of the literature (20 references), the authors find DM associated with the most varied malignancies: stomach, breast, ovary, lung, colon, rectum, gallbladder, kidney, uterus, larynx, leukemia, cervix uteri, vagina, esophagus, sarcoma, plasmacytoma, etc. Including children, some authors report a 50% incidence of DM in relation to cancer, with the association of DM and breast cancer occupying second place according to frequency.

64-1398 CUTANEOUS LYMPHOGRANULOMA IN A SUBJECT EXPOSED TO LOCAL IRRITANTS. (It.) Illini, G. (Inst. Occupat. Med., U. Pavia, Italy) and P. Seghizzi. Gior. Clin. Med. 45(3):217-225, 1964.

Case of Hodgkin's disease is described in a 1-year-old male field hand with a long-standing history of cutaneous allergy and severe diffuse dermatitis, ulcerations, and axillary and inguinal adenopathies. It is suggested that the cutaneous hypersensitivity of this pt. was the determining factor in the primary localization of Hodgkin's disease in the skin.

64-1399 CANCER CURES AND SPONTANEOUS REGRESSIONS. (Fr.) Fauvet, J. (Gustave-Roussy Inst., Villejuif/Seine, France), J. Roujeau and R. Piet. Rev. Prat. 14(17):2177-2180, 1964.

After reviewing (7 references) 26 cases of cancer spontaneous regression published in the literature from 1958 to 1963, the authors describe two personal cases. A 19-year-old woman was discharged with ascites and in terminal condition approx. 1.5 yr. after bilateral oophorectomy for an ovarian teratoma but improved rapidly and was in good condition 8 yr. later. In a 7-year-old boy with

Hodgkin's disease, a short episode of icterus with fever was followed by the complete disappearance of peripheral and mediastinal adenopathies (otherwise resistant to prednisone) and the remission lasted 3 yr.

64-1400 ANOTHER FOLLOW-UP STUDY OF CHILDREN BORN OF MOTHERS WITH LEUKEMIA. (E.) Ask-Upmark, E. (Dept. Med., Roy. U. Hosp. Upsala, Sweden). Acta Med. Scand. 175(3):391-394, 1964.

Follow-up studies for 9-41 yr. have been conducted on 6 children, born of 3 mothers with leukemia. The Italian and Norwegian mothers had chronic myeloid leukemia, and the Swedish mother had acute myeloid leukemia. One boy (Norwegian) died from "malignancy" at the age of 9. The remaining 5 were alive and well: one boy and one girl (twins, Italians) after 10 yr.; one boy (Norwegian) and one girl (Swedish) after 41 yr., and one girl (Norwegian) after 36 yr. These follow-ups represent the longest recorded in the literature for children born of leukemic mothers.

64-1401 EXAMINATION OF THE TUMOR-INDUCING EFFECT IN RATS OF METAL DIFFUSION CHAMBERS. (Ger., Abstract) Teichmann, B. (Robert-Rossle Clin., German Acad. Sci. Berlin). Naturwissenschaften 51(12):294-295, 1964.

Sprague-Dawley rats (SDR) and Wistar rats (WR) were implanted with a metal chamber: 10 SDR and 10 WR i.p., and 10 SDR and 10 WR s.c.. No pathologic changes were noted in 5 rats that died after 194-302 days. In survivors, chambers were removed after 380 days and were observed for another 150 days. No tumor formation was found.

64-1402 CHANGES IN THE CHROMOSOME SETS OF HETEROLOGOUSLY GROWING TUMORS. (Ger.) Wrba, H. (Inst. Path., U. Munich, Germany), J. Eicke and M. L. Meiners. Zschr. Krebsforsch. 66(2):115-118, 1964.

Karyotypes of Walker carcinoma cells were studied in rats (120-130 passages), golden hamsters (>30 passages) and mice (40-50 passages). In all 3 animal species, the max. chromosome number was 63 (62-65), which corresponds to the triploid set of the rat. In the tumor mitoses of all 3 a sub-metacentric marker chromosome with heterochromatic segments was found. The numbers of this chromosome found in dividing cells were: rat, 61%; hamster, 63%; mouse, 78%. It occurs independently of the number of chromosomes, and occasionally appears in haploid cells. The morphology of this marker chromosome was identical in all 3 species.

64-1403 OBSERVATIONS ON AFRICAN MACROGLOBULINEMIA. (Fr.) Sandor, G. (Pasteur Inst., Paris), G. Charmot and R. Vargues. Presse Med. 72(23):1353-1356, 1964.

On the basis of 32 serologically confirmed cases, African macroglobulinemia (AM; 14 new cases, 18 previously published) is considered distinct from Waldenström's macroglobulinemia based on diagnostic features such as splenomegaly, occasional hepatomegaly, chronicity, and distinct cytological and serological findings. Although all of the AM pts. examined were colored (11 males, 3 females) the racial factor is not considered decisive in the etiology of this type of dysproteinemia, but a greater reactivity of the RES in colored subjects is not ruled out.

64-1404 CHROMOSOME STUDIES IN WALDENSTRÖM'S DISEASE. (Ger.) Braunsteiner, H. (2nd Dept. Med., U. Vienna, Austria), G. Rothenbuchner and B. Schober. Wien. Klin. Wschr. 76(27/28):502-503, 1964.

In a 66-year-old man with Waldenström's disease, both of whose parents had died of gastric carcinomas in their 70's, chromosome numbers of 43, 44, 45, 46 and 47 were demonstrated in 4, 6, 10, 124 and 2 cells, resp., of a total of 146 metaphases studies in a sample of peripheral blood. Among cells with normal chromosome numbers, dissimilar pairs were seen in 2/37 metaphases in a peripheral blood sample and in 4/4 metaphases in a direct bone marrow sample. Long, drawn-out centromeres were also seen in Chromosome Groups A and B (I and II) (more frequently in A). In a brief review (10 references) of the literature, it is stated that changes in chromosome number are not an invariable accompaniment of Waldenström's disease.

64-1405 THE BEHAVIOR OF THE NUCLEOLI OF LIVER CELLS IN THIOACETAMIDE POISONING. (Ger.) Kendrey, G. (1st Inst. Path., U. Leipzig, Germany). Acta Morph. Acad. Sci. Hung. 12(4):407-413, 1964.

Male Wistar rats given thioacetamide (25 mg/kg in physiological saline, i.p., x 14 in 16 days) showed strongly pyroninophilic nucleoli which migrated to the nuclear membrane and, in some cases, through the membrane into the cytoplasm. In a few cases the nucleoli migrated out of the cells into the intercellular spaces. It is suggested that the histological and histochemical changes observed are related to those which occur in the early stages of carcinogenesis after admin. of a carcinogenic substance.

64-1406 MULTIPLE CUTANEOUS LEIOMYOMA IN IDENTICAL TWINS. (E.) Rudner, E. J. (Dept. Derm., Wayne State U. Coll. Med., Detroit, Mich.), O. D. Schwartz and J. N. Grekin. Arch. Derm. (Chicago) 90(1):81-82, 1964.

This is believed to be the first report of multiple cutaneous leiomyoma in a pair of identical twins (women; age 52 yr.). Both women had

undergone hysterectomies at the age of 40 yr. The uterine tissue removed was microscopically diagnosed as degenerating myomata uteri and leiomyofibromata.

64-1407 CARCINOMA DEVELOPING IN A PRE-EXISTING SCAR. A CASE REPORT OF CARCINOMA OF AMPUTATION STUMP. (E.) Wilhite, J. L. (Dept. Surg., Roanoke Mem. Hosp., Va.). Virginia Med. Monthly 91(6):292-294, 1964.

Biopsy of granulation tissue taken from an intermittently infected thigh stump (amputation performed in 1917) of a 75-year-old man revealed a well differentiated squamous cell carcinoma.

64-1408 SURGICAL OBSERVATIONS OF CANCER OF THE STOMACH ASSOCIATED WITH GASTRIC ULCER OR GASTRITIS. (Jap.) Iguchi, K. (2nd Dept. Surg., Kyushu U. Sch. Med., Japan). Fukuoka Igaku Zasshi (Fukuoka Acta Med.) 54(6):708-711, 1963.

In a series of 39 specimens resected in the author's clinic, findings suggestive of chronic atrophic hyperplastic gastritis were found in 25 (59%). In another series of 40 specimens of carcinoma of the stomach, 87% showed metaplasia of the gastric mucosa. From these series and others it is concluded that there is a high frequency of a benign type of ulceration of the mucosa in the presence of carcinoma of the stomach.

64-1409 AUTORADIOGRAPHIC ANALYSIS OF UPTAKE OF TRITIATED THYMIDINE AND S^{35} CYSTINE BY CULTURED HUMAN CERVICAL EXPLANTS UNDERGOING METAPLASIA. (E.) Reid, B. L. (Queen Elizabeth II Res. Inst., U. Sydney, N.S.W., Australia). J. Nat. Cancer Inst. 32(5):1059-1073, 1964.

Biopsy specimens of cervical tissue undergoing metaplasia removed from the squamocolumnar junction of 52 normal, healthy women at the 6th to 7th postnatal wk. were divided and one fragment was exposed to H^3 -thymidine, the other to S^{35} cystine for 4 hr. Tritiated thymidine uptake occurred in approx. 5% of normal squamous epithelium cells; that in metaplastic squamous epithelium was variable and of about the same degree but with occasional specimens showing a much higher percentage; exposed columnar epithelium had <1% incorporating; deeper columnar epithelium did not incorporate. Distribution of S^{35} cystine in plasma cells paralleled that of stains for SH groups.

64-1410 TUMOR OF THE THYROID AND ADRENAL IN GERM-FREE MOUSE. (Jap., Abstract) Uno, H. (Dept. Path., Nagoya U. Sch. Med., Japan), Y. Kamii and M. Miyagawa. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Jap.) 52:109-110, 1963.

Ultimobranchial cysts were found in the thyroid gland of 28/30 Swiss mice raised in a germ-free

environment compared to 42/44 raised in a conventional environment. Marked proliferation was observed in 7/30 germfree mice compared to 6/44 controls. The incidence of such cysts in C3H mice was 28/28 in germfree mice (11/28 showing marked proliferation) and 7/8 in controls (1/8 showing marked proliferation). Tumor of the thyroid was found in 21/28 C3H mice (400-1,000 days old) raised in a germfree environment and in 3/9 controls. Also in this strain, 30/41 germfree mice developed lipoid adenoma of the adrenal gland, compared to 9/13 in conventional mice.

64-1411 HISTOCOMPATIBILITY VARIATIONS IN MOUSE TUMOR CELLS AND EMBRYONIC TISSUE WITH THE USE OF C57BL/10Sn STRAIN AND ITS ISOGENIC RESISTANT STRAINS. (E.) Dhaliwal, S. S. (Dept. Zool., U. Malaya, Kuala Lumpur). *J. Nat. Cancer Inst.* 32(5):1001-1022, 1964.

X-ray-induced lymphomas and 20-methylcholanthrene-induced sarcomas in hybrid mice between C57BL/10Sn and its isogenic resistant (IR) strains (shown to be coisogenic) were used for the study of histocompatibility variants in mouse tumor cells. All sarcoma and lymphomas tested produced variants when transplanted in the parental strains and no parental strain was favored. Variants were highly specific and stable; their number differed from generation to generation and according to the tumor subline used and decreased with reduction of the inoculum. Cytological studies revealed hyperploidy in large numbers of cells of the variants. It is concluded that tumors are not good material for the study of somatic mutations, due to their cytological instability and difference in transplantation behavior. The use of embryonic tissue for detection of histocompatibility mutations was investigated. Because small numbers of embryonic cells transplanted into adult mice were difficult to grow, the method was considered unsuitable. (See also the following abstract.)

64-1412 USE OF "IMMUNOLOGICAL ENHANCEMENT" IN THE STUDY OF HISTOCOMPATIBILITY MUTATIONS. (E.) Dhaliwal, S. S. (Dept. Zool., U. Malaya, Kuala Lumpur). *J. Nat. Cancer Inst.* 32(6):1245-1258, 1964.

Immunologic enhancement of tumor homografts was used to detect histocompatibility mutations at the histocompatibility-2 (H-2) locus in C57BL/10Sn mice and its isogenic resistant (IR) strains. Of the host-tumor combinations used, BA/1 was best for use in enhancement, giving almost 100% takes. No difference was found between various sarcomas. Complete specificity was lacking for strains C57BL and B10.D2 with active immunization. With passive immunization, anti-B10.D2 serum enhanced B10.D2 strain tumors markedly and C57BL strain partially; anti-C57BL serum enhanced only C57BL tumors. In tumor cell mixtures, anti-C57BL serum was found to enhance

a small number of C57BL tumor cells in a large inoculum of B10.D2 cells, whereas anti-B10.D2 serum enhanced both C57BL and B10.D2 cells. Unlike B10.D2 strain, a third IR strain, B10.M, showed complete specificity for enhancement. Hybrid tumors of (C57BL x B10.D2)F1 were enhanced with anti-B10.D2 serum and not with anti-C57BL serum; hybrid tumors of (C57BL x B10.M)F1 were enhanced only when host mice were conditioned with antisera to both strains. A method of detection of mutations with enhancement is presented. A large number of cells were tested by this method, but no mutant variants were isolated. The lack of complete specificity for enhancement between some of the IR strains indicates that enhancement is not suitable for the study of mutations at the H-2 locus. (See also the preceding abstract.)

64-1413 SUSCEPTIBILITY OF INJURED TISSUES TO HEMATOGENOUS METASTASES: AN EXPERIMENTAL STUDY. (E.) Alexander, J. W. (Dept. Surg., U. Cincinnati Coll. Med., Ohio) and W. A. Altemeier. *Ann. Surg.* 159(6):933-944, 1964.

Splenic trauma was induced in 30 domestic rabbits (2.5-3.5 kg wt.) by inj. of nitrogen mustard (0.07 mg/kg) into a gastric branch of the splenic artery during vascular isolation of the spleen. The circulation was restored and, immediately following or 2-37 days later, the animals were inoc. intraarterially with VX-2 carcinoma (0.5-8.1 x 10⁶ cells). At sacrifice, during the 4th wk. after tumor inoc. 67% of the test animals developed splenic and perisplenic metastases compared to only 8% of controls. A 20-fold increase in metastases was noted in the area of surgical incision. Intestinal metastases increased in animals following intra-abdominal manipulation. The increase of metastases in injured tissues was not a result of a stress phenomenon: the number of metastases in uninjured tissues in test animals was only slightly greater than that in comparable tissues in controls. An increase in metastases was noted in groups inoc. with tumor cells before or after abdominal incision, and after induced temporary (3-5 hours) splenic ischemia. The increase in metastases was not prevented by the use of iodized or chromicized catgut for wound closure or by i.v. inj. of low molecular wt. dextran.

64-1414 DNA CONTENTS OF CHROMOSOME PH¹ AND CHROMOSOME 21 IN HUMAN CHRONIC GRANULOCYTIC LEUKEMIA. (E.) Rudkin, G. T. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.), D. A. Hungerford and P. C. Nowell. *Science* 144(1):1229-1231, 1964.

Microspectrophotometric analysis of chromosomes from a 68-year-old female in the early stages of chronic granulocytic leukemia following treatment for 8 days with busulfan showed the DNA content of chromosome Ph¹ was 61% that of chromosome 21 or 22. All metaphase stages contained this characteristic Ph¹ chromosome. The difference

in DNA content between this abnormal and the normal chromosome from which it is believed to be derived represents 0.5% of a diploid chromosome complement (i.e., 2×10^7 nucleotide pairs). The method used was not sensitive enough to determine the exact fate of this portion.

64-1415 PROLONGED CULTURE OF DIPLOID HUMAN CELLS. (E.) Miles, C. P. (Dept. Path., Stanford Sch. Med., Palo Alto, Cal.). Cancer Res. 24(6):1070-1081, 1964.

Neither spontaneous transformation, chromosome complement alteration nor sex chromatin changes (female) occurred in 44 diploid human cell strains derived from skin (infant, child and adult), thyroid (adult) and amnion. These cultures were maintained up to 9 mo. (av. 4 mo.) and 26 passages, then, generally spontaneous degeneration followed which was characterized by accumulation of fine granules on the cell surfaces. The doubling time for fibroblasts was 4-5 days. Epithelioid growth was also found in the thyroid cultures.

64-1416 SUBMETACENTRIC CHROMOSOME IN CHRONIC MYELOCYTIC LEUKEMIA. (E.) Goh, K.-O. (Dept. Med., U. Rochester Sch. Med. Dent., N. Y.), S. N. Swisher and S. B. Troup. Arch. Intern. Med. (Chicago) 114(3):439-443, 1964.

Chromosome analysis in an 80-year-old woman with chronic myeloid leukemia with prior therapy with busulfan showed in addition to the typical Ph¹ chromosome an additional submetacentric chromosome of medium size resembling the chromosomes of the 6-12 and X group. The cells with this additional chromosome decreased after treatment with busulfan, and the pt. developed a clinical remission.

64-1417 SPONTANEOUS REGRESSION OF PRIMARY BILE DUCT CARCINOMA. (E.) Legier, J. F. (Riverside Hosp., Newport News, Va.). Cancer 17(6):730-732, 1964.

A primary bile duct carcinoma in a 57-year-old male pt. involved the pancreas and regional lymph nodes. The pt. died 3 yr. later of cerebellar metastases; however, during this interim the liver reduced in size and the pt. was in good health. Microscopic examination at autopsy revealed a scarred liver lobe with no traces of the

primary tumor nor of the neighboring metastases. An immunological mechanism of action is discussed.

64-1418 CYTOLOGICAL STUDIES OF TUMORS. XL. CHROMOSOME STUDIES IN FIFTY-TWO HUMAN TUMORS. (E.) Makino, S. (Inst. Zool., Hokkaido U., Sapporo, Japan), M. S. Sasaki and A. Tomomura. J. Nat. Cancer Inst. 32(4):741-777, 1964.

Using the water-pretreatment acetic dahlia squash method, chromosomes were investigated in 52 human tumors (carcinoma of the stomach 30, uterus 13, rectum 4, breast 2, ovary 2 and ascites hepatoma 1). Detailed chromosome analyses were made of 37 tumors, of which 34 were characterized by 1, or rarely 2, marked stemlines with a characteristic number mode (or modes) and a specific karyotype (or karyotypes), while 3 tumors showed karyological heterogeneity, with a wide distribution of chromosome numbers. Tumors characterized by the hyperdiploid-triploid modality were most frequent, the hypotetraploid one ranking next. No definite correlation was detected between the chromosome condition of tumor cells and pathological pattern of the tumor itself. It appeared that the genetic pattern, which is closely correlated with the property of the tumor, may not be identical among tumors, even though they originate from the same organ. It was concluded that heteroploid transformation of cells may be an important factor in malignant transformation, in addition to numerical alteration and/or structural reorganization of chromosomes.

64-1419 STUDIES OF POLYENIC FATTY ACIDS IN TUMORS AND TUMOR-BEARING ANIMALS. (Ger.) Ostertag, H. (Coll. Gen. Social Hygiene, Hamburg, Germany) and J. Wurziger. Arch. Hyg. Bakt. 148(4-5):261-270, 1964.

In C₃H mice with spontaneous mammary cancers and in rats bearing Jensen sarcoma, Walker carcinoma or spontaneous tumors induced by s.c. inj. of vesicant soya oil, both the refractive index and the content of arachidonic acid were shown to increase progressively with increased age and growth of the tumors, as determined in petroleum ether extracts of tumor tissue or of normal tissue. Concurrently, the content of linolenic acid decreased progressively to the point of disappearance. The authors conclude that these phenomena appear to be significant, especially in view of the present lack of understanding of linolenic acid's biologic effects and mechanism of action.

ERRATUM:

2(4):#654, 1964. Correct beginning of last sentence to read: After i.v. admin. methylnitrosourea (not NU) resulted in carcinoma of the lung, showing.....

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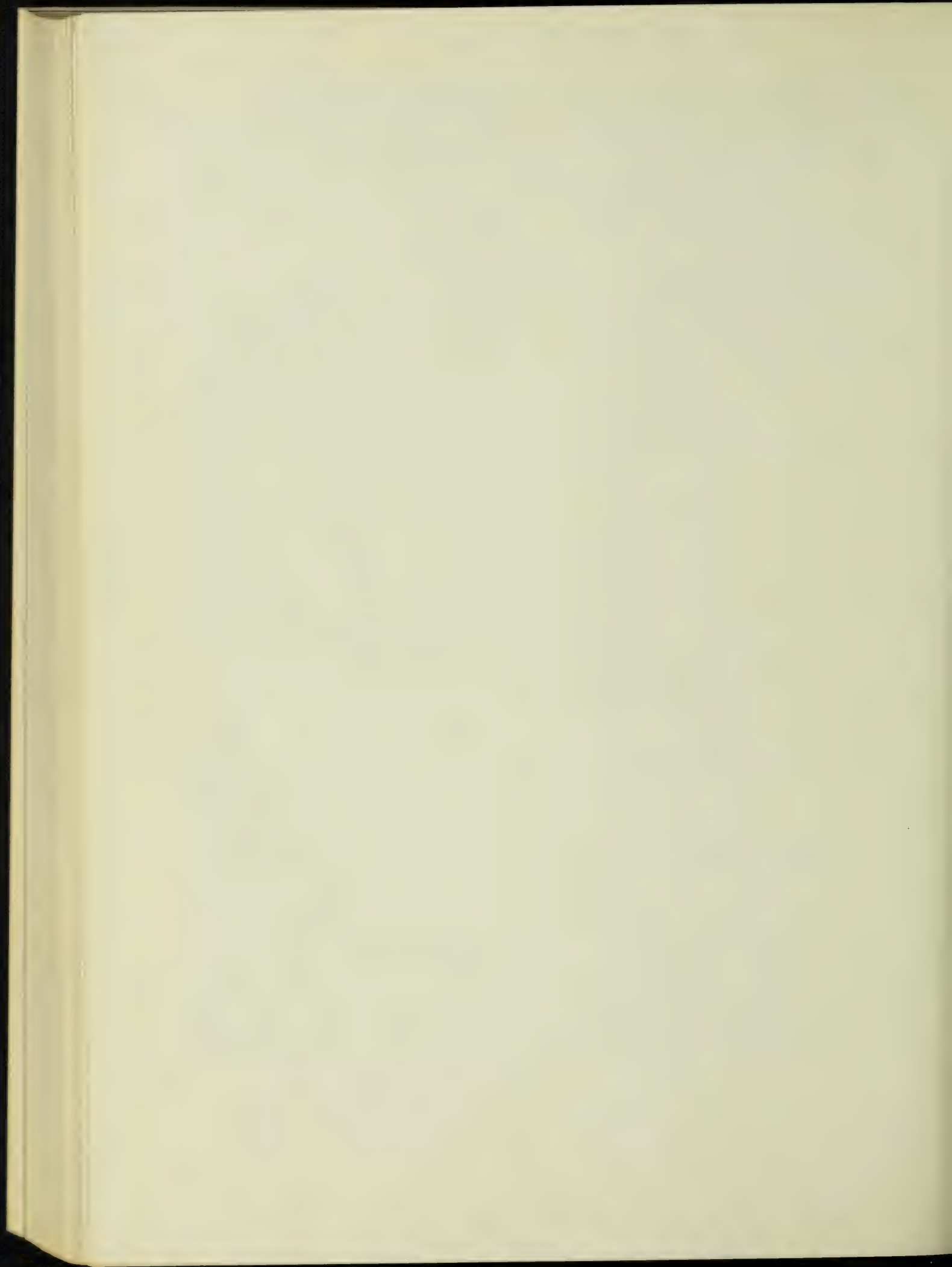
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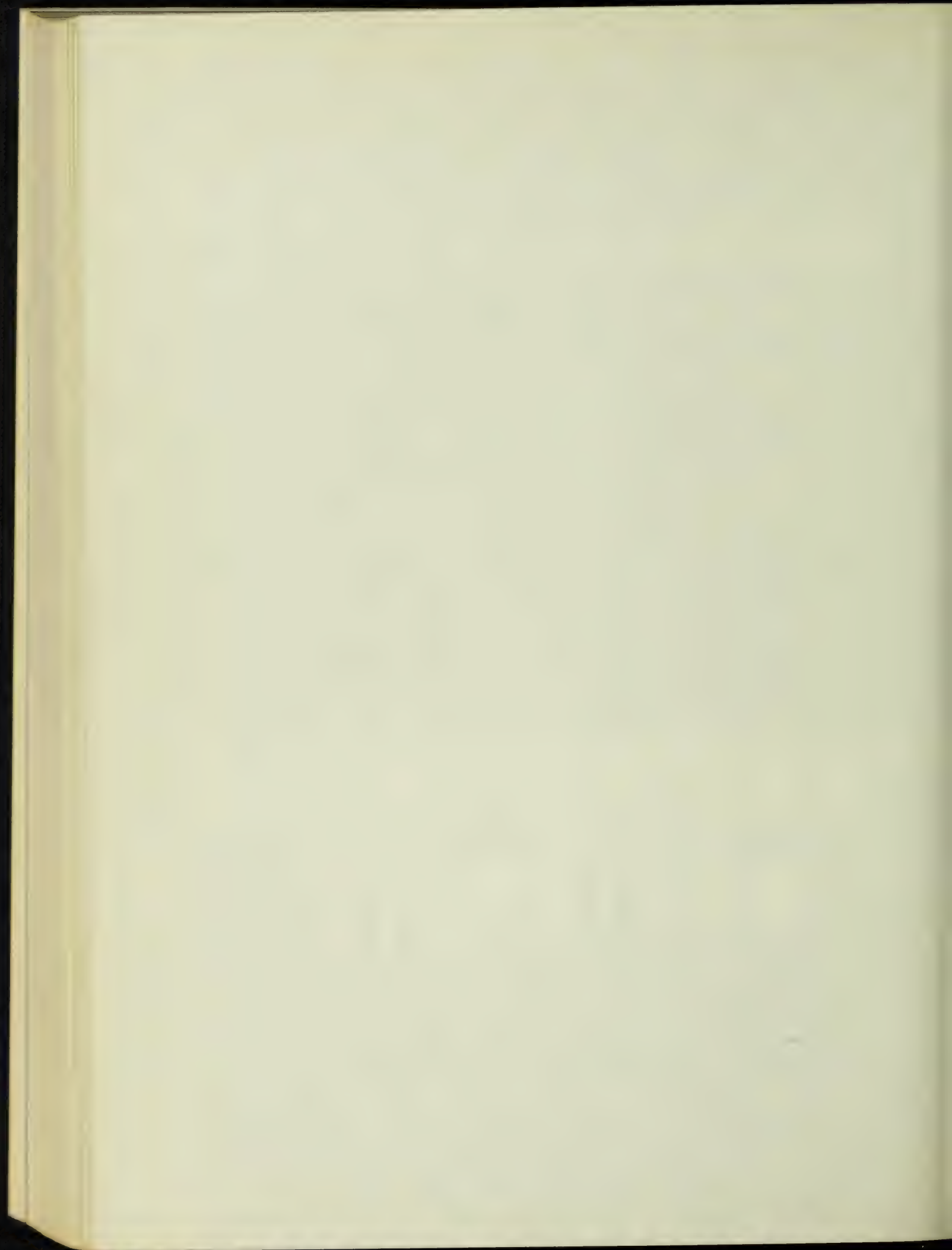
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CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service



CARCINOGENESIS ABSTRACTS

Volume 2, Number 8
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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work. Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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NOTE

Journal names are abbreviated according to the list of abbreviations used by Index Medicus. If the journal is not covered by Index Medicus, then the abbreviations (with some modifications) found in World Medical Periodicals, 3rd Edition, are used.

ABBREVIATIONS USED IN ABSTRACTS

admin.	administered, administration	max.	maximum, maximal
approx.	approximately	mg	milligram(s)
av.	average	min.	minute(s)
C	curie(s)	ml	milliliter(s)
mC, μ C	milli-, microcurie(s)	mm	millimeter(s)
cm	centimeter(s)	mo.	month(s)
conc.	concentrate(d), concentration(s)	MTD	maximum tolerated dose
cpm	counts per minute	NCI	National Cancer Institute
DNA	deoxyribonucleic acid	NIH	National Institutes of Health
DNase	deoxyribonuclease	p.o.	orally
e.g.	for example	PFU	plaque forming unit(s)
FFU	focus forming unit(s)	ppm	parts per million
g	gram(s)	pt(s).	patient(s)
μ g	microgram(s)	RBC	red blood cells (erythrocytes)
g.i.	gastrointestinal	RES	reticuloendothelial system
Hb	hemoglobin	resp.	respectively
hr.	hour(s)	RNA	ribonucleic acid
ID ₅₀	median infectious dose	RNase	ribonuclease
i.m.	intramuscular	s.c.	subcutaneous
incub.	incubated(d), incubation	soln.	solution(s)
inj.	injected, injection(s)	TCID	tissue culture infectious dose
inoc.	inoculated, inoculation(s)	x	times (e.g. x 3/wk.)
i.p.	intraperitoneal	U	unit(s)
I.U.	international unit(s)	UV	ultraviolet
i.v.	intravenous	VA	Veterans Administration
kg	kilogram(s)	vol.	volume
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes) or count
m	meter(s)	wk.	week(s)
M	molar	wt.	weight(s)
mM, μ M	milli-, micromolar	yr.	year(s)

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	E.	English	Hun.	Hungarian	Lith.	Lithuanian	Ser.	Serbo-Croatian
Ar.	Arabic	Eston.	Estonian	ic.	Icelandic	Maced.	Macedonian	Sl.	Slovene
Bul.	Bulgarian	Fin.	Finnish	In.	Indonesian	Nor.	Norwegian	Sp.	Spanish
Ch.	Chinese	Fr.	French	It.	Italian	Pol.	Polish	Sw.	Swedish
Cz.	Czech	Ger.	German	Jap.	Japanese	Por.	Portuguese	Th.	Thai
Dan.	Danish	Gr.	Greek	Kor.	Korean	Rum.	Rumanian	Uk.	Ukrainian
Dut.	Dutch	Heb.	Hebrew	Latv.	Latvian	Rus.	Russian	Viet.	Vietnamese

REVIEW

- 64-1420 VIRUSES AS POSSIBLE ETIOLOGIC CAUS OF TUMORS IN MAN. (Heb.) Cohen, A. Harefuah 66(8):266-267, 1964.

In a brief review of the recent literature implicating viruses as oncogenic agents in man, some of several lines of experimental evidence mentioned are: the prompt induction of fatal leukemia in mice inj. with brain tissue from pts. who died of leukemia; malignant transformation, in tissue culture, of human embryonic kidney by SV40; induction of tumors in hamsters and mice; the nucleotides of the DNA of adenoviruses 12 & 18 of man differs from those of other adenovirus DNA; serologic evidence implicating adenovirus in the induction of human tumors; the electron microscopic demonstration of myxovirus-like particles in the plasma of leukemic children. (29 references)

- 64-1421 MALIGNANCY AND ARSENIC KERATOSIS, ACANTHOSIS NIGRICANS, BOWEN'S DISEASE AND MYCOSIS FUNGOIDES. (Fin.) Niemi, K.-M. Duodecim 79(21):896-900, 1963.

The author reviews some of the etiology, the histogenesis, and symptomology of arsenical keratosis, Bowen's disease, acanthosis nigricans and mycosis fungoides, considered as precancerous skin diseases. (6 references)

- 64-1422 PSYCHE--NERVOUS SYSTEM--NEOPLASTIC PROCESS: AN OLD PROBLEM WITH NEW INTEREST. PART II: NEURAL RELATIONS. (Ger.) Altrusch, H.-J. F. (19 Babenend St., Oldenburg Oldb.), Germany). Zschr. Psychosom. Med. 10(1):1-10, 1964.

A continuation of CRA 2(2):#165, 1964 is presented and consists of a review of the etiologic role of the nervous and hormonal systems and of various biologic secretions and products in neoplastic diseases. (See also CRA 2(2):#376, 1964.) (10 references)

- 64-1423 CLINICAL--STATISTICAL STUDIES RELATING TO CURRENT PROBLEMS IN TERATOLOGY. A REVIEW. (Ger.) Sievers, G. ("Chemie Grunenthal m.b.H.", Stolberg, Rhineland, Germany). Arzneimittelforschung 14(6):605-655, 1964.

An extensive review of the classification, incidence and presumed etiology of teratogenic defects is accompanied by a detailed statistical study of the incidence of malformations of the unborn in the Federal German Republic between 1960-62 and of all known, possible etiologic influences. It is also accompanied by a summary of previously published reports on the possible effects of thalidomide. The author states that no definite conclusion can be reached as to whether

this drug has any effect on blastogenesis, embryogenesis, a previously damaged embryo or the pregnant mother. If a potential deleterious effect is assumed, the potential risk must be estimated at approx. 5%--in contrast to a potential hereditary risk of 12% in families with a history of serious congenital malformation(s) of the extremities. He concludes that the assumption that thalidomide can be solely responsible for malformations of the extremities cannot be supported, either theoretically or statistically. (Approx. 300 references)

- 64-1424 VIRUSES AS ETIOLOGIC AGENTS IN ACUTE LEUKEMIA. (E.) Grace, J. T., Jr. (Roswell Park Mem. Inst., Buffalo, N. Y.). CA 14(4):135-138, 1964.

This brief review covers early work on murine and fowl viruses and the additional evidence from use of the electron microscope; these findings plus the fact that leukemia viruses have been found in other animals have provided a hypothetical basis for the etiology of human leukemia and have also defined the methodology for detecting such viruses in animals. (13 references)

- 64-1425 OCCUPATIONAL DISEASES. A GUIDE TO THEIR RECOGNITION. (Public Health Serv. Publ. No. 1097.) Gafaer, W. M. (Ed.). U.S. Govt. Printing Office, Washington, D. C., 375 pp., 1964.

After some general considerations and a section on occupational dermatoses and another on pneumoconioses, sections deal with various aspects of exposure to chemicals, pesticides, plastics and synthetic resins, physical, biologic, and plant and wood hazards. Systemic effects described include neoplasms and premalignant lesions, where these are clinical problems. Under specific agents are also listed potential occupational exposures. (References follow each agent or in some cases discussion of a type of hazard.)

- 64-1426 "TWO-STAGE MECHANISM" OF CARCINOGENESIS AS AN ANALYTIC TOOL. (Sp.) Trainin, N. (Weizmann Sci. Inst., Rehovoth, Israel). Rev. Fac. Cienc. Med. Cordoba 21(4):291-303, 1963.

In a review of previously published personal work, some of which has already been reported in CRA 2(6):#1041, 1964, the author applies the concept of a 2-stage mechanism in carcinogenesis to urethan and its role in radiation-induced leukemogenesis. The author considers radiation as initiator and urethan as promoter in a 2-stage process of leukemogenesis. He found that tissues from irradiated mice or even mouse tissues irradiated "in vitro" contained a "transmissible factor" which, when inj. into normal mice

subsequently treated with urethan, caused a high percentage of leukemias. Possible interpretations of the nature of this factor included: a dormant tumor cell, an inactive or incomplete virus, or a chemical compound (metabolite of radiation).

- 64-1427 DEATHS FROM SMOKING. (E.) Editorial. *Brit. Med. J.* 1:1451-1452, 1964.

This editorial discussion on the causative effect of cigarette smoking and lung cancer cites the study year made by Doll and Hill on mortality among British doctors and their smoking habits (see CRA 2(8):#1563 and #1564, 1964). In those who smoked, the mortality was 20% greater than in nonsmokers. The excess mortality was as high as 63% in those who smoked more than 25 cigarettes a day, but only 1% in pipe and cigar smokers. The mortality rate was slightly higher in the urban areas. The socio-psychological aspects of smoking, and the establishment of anti-smoking clinics are also discussed. (14 references)

- 64-1428 IMMUNOLOGIC ASPECTS OF HODGKIN'S DISEASE. (E.) Aisenberg, A. C. (Massachusetts Gen. Hosp., Boston). *Medicine (Balt.)* 43(3):189-193, 1964.

In a review of the literature, the cutaneous anergy and the conservation of antibody formation against most antigens observed in subjects with Hodgkin's disease are considered in a discussion of the immunologic aspects of this disease. The relationship to Hodgkin's disease of two new wasting diseases of lymphoid tissue, the graft-versus-host reaction and the wasting disease observed in thymectomized animals, is also discussed. (51 references)

- 64-1429 THE GROUP OF PAPOVA VIRUSES, AND IN PARTICULAR SIMIAN VIRUS SV-40. (Rum.) Melnick, J. L. *Stud. Cercet. Inframicrobiol.* 15(1):3-14, 1964.

See CRA 2(3):#414, 1964. (18 references)

- 64-1430 PRESENT INFORMATION ON GENETICAL AND SOMATIC EFFECTS OF RADIATION. (E.) Biagini, C. (Inst. Radiol., U. Rome). *Minerva Nucl.* 8(4):203-207, 1964.

A short review is presented of the biological effects of radiation (mammals and humans) and the various factors involved: dose (total or cumulative), distribution of doses in tissues and in relation to time, age and physiological conditions of the irradiated subject. Also reviewed are reports of effects relative to cancer and leukemia. A table is presented of dose levels of possible biological significance for various adult and embryonic tissues and systems. (12 references)

- 64-1431 POST-IRRADIATION OSTEOPATHY. (E.) Salib, P. I. (Orthopedic Dept., Massachusetts Gen. Hosp., Boston). *Am. J. Orthop.* 6(5):122-125, 1964.

In a review of the skeletal effects of irradiation, the author states that post-irradiation sarcomas are most common after exposure to internal irradiation with an incidence of about 20% and most frequent localization around the hip or knee. The latent period is given as 5-10 yr., in contrast to 3-20 yr. following exposure to external irradiation. The max. permissible internal deposit is said to be equivalent to 0.1 µg retained radium, while all sarcomas are said to have involved the retention of an equivalent of 0.5 µg radium or more. The amount of external irradiation required to induce sarcomatous changes is said to be (usually) 3,000 r or more. Some benign lesions have been known to become malignant following irradiation exposure and 14% of persons in their 50's who have retained radium in their bodies for approx. 25 yr. are said to develop sarcomas. (11 references)

- 64-1432 AUTOIMMUNITY AND CHROMOSOMAL ABERRATIONS. (E.) Burch, P. R. J. (U. Leeds, England), R. G. Burwell and N. R. Rowell. *Lancet* 1:720, 1964.

In a brief review and discussion of the work of the author and others on chromosomal aberrations and their significance in autoimmunity, the connection (see CRA 1(3):#371, 1963) of chromosome 21 with chronic myeloid and lymphatic leukemia and with the high incidence of leukemia and infections in Down's syndrome is proposed as reflecting a possible common biological principle. In leukemogenesis and carcinogenesis, it has been suggested that the tissue coding factor becomes autoantigenic as the result of somatic mutation in the "target" cell (see CRA 1(3):#372, 1963). Thus, aneuploidy in malignant cells and chromosomal abnormalities (e.g., Ph1) might well be the result of an autoimmune reaction between "disturbed antigen" deoxyribonucleoproteins and diffusible normal mitotic control proteins. Disturbed tolerance and disturbed antigen relationships should then both produce chromosomal abnormalities. (14 references)

- 64-1433 ALTERATIONS IN BIOLOGICAL PATTERNS OF CELLS AS RELATED TO GENETIC ENZYME DEFECTS. (E.) Kalckar, H. M. (Biochem. Res. Lab., Massachusetts Gen. Hosp., Boston). *Perspect. Biol. Med.* 7(4):471-483, 1964.

In a review of metabolic and chemical patterns as related to malignant growth, the author discusses the alterations of surface lipopolysaccharide protein complexes resulting in a cellular deletion in antigen pattern as a possible basis for cancer growth. The loss of an antigen may be brought about by gene mutations or by the addition of

foreign genes, such as episomes or viruses. The biochemical changes involved are numerous, and it will be difficult to definitely implicate a chemical or metabolic alteration as a primary basis for the development of malignancy. (See also CRA 1(12):#2222; *ibid.*, 2(1):#70, 1964.) (51 references)

- 64-1434 PROCEEDINGS OF THE 85TH JOINT SESSION OF MOSCOW AND MOSCOW REGION SCIENTIFIC ONCOLOGICAL SOCIETY AND HEMATOLOGY SECTION OF THE MOSCOW THERAPEUTIC SOCIETY HELD ON MAY 28, 1963. (Rus.) Milonov, B. V. and E. A. Rabinovitch. *Vop. Onkol.* 10(4):110-112, 1964.

The participants in the discussion on etiology and pathogenesis of leukemia have mentioned the role of cell-free agents (DNA), the Philadelphia chromosome, radiation and viruses. Leukemogenic properties of some intermediate products of metabolism (such as those of tryptophan) were confirmed. The significance of the character of food in the development of leukemia was discussed. The theory of viral etiology should be reexamined in view of the fact that polyoma virus can produce 30 varieties of tumors in various species. While viruses are definitely related to leukemia in the mouse and chicken, no such relationship exists with human leukemia. (No references)

- 64-1435 CARCINOGENIC AND CHRONIC TOXIC HAZARDS OF AROMATIC AMINES. (E.) Scott, T. S. (U. Manchester, England). Elsevier Monographs on Toxic Agents. Browning, E. (Ed.). Elsevier Publ. Co., Amsterdam, 208 pp., 1962.

After a brief historical review on the chemistry, acute toxicity and industrial uses of aromatic amines, the history of the occurrence of occupational tumors of the bladder is reviewed, starting with the report in 1895 of three verified cases of tumor of the bladder in men who had worked for 15, 20 and 29 yr. in the fuchsin industry, and following the occurrence of this disease through the succeeding yr. and in various countries. A chapter is devoted to the consideration, individually, of the various compounds which have been suspected or proved capable of causing occupational tumors; these include fuchsin, aniline, benzidine, α - and β -naphthylamine, auramine, xenylamine, diphenylamine as well as some other compounds. Later chapters cover the natural history of 'papilloma of the bladder', various measures for its prevention by special protective measures and work practices as well as methods of handling materials. One chapter is devoted to the technical considerations of prevention of carcinogenesis by certain specific compounds, the most hazardous of which is β -naphthylamine. The manufacture of β -naphthylamine in Great Britain was halted in 1952, but it is still manufactured in the U.S., Italy, Czechoslovakia and Japan. Finally, the legal aspects and the future of such carcinogenic compounds are discussed, particularly with reference to Great Britain.

- 64-1436 HUMAN TUMOURS SECRETING CATECHOLAMINES. CLINICAL AND PHYSIOPATHOLOGICAL STUDY OF THE PHEOCHROMOCYTOMAS. (E.) Herman, H. (Fac. Med., Lyon, France) and R. Mornex. *Internatl. Ser. Monographs on Pure and Appl. Biol. Div.: Modern Trends in Physiological Sciences.* Vol. 23. Alexander, P. and Z. M. Bacq. (Eds.). Macmillan Co., New York, 1964, 207 pp. illus.

A comprehensive monograph on the clinical and physiopathological aspects of the pheochromocytomas, including 507 well-documented cases (the authors' and from the literature). Of particular interest are the details given for 12 families in which pheochromocytomas were inherited as a dominant. The association of pheochromocytoma with Recklinghausen's disease in 31/507 cases is analyzed. The nature of the disease in children is described; of 66 cases which ran their course entirely during childhood (14 yr. for girls and 15 yr. for boys), the frequency was higher in boys than in girls (44 to 22). The development of a malignant tumor in any location in a pt. bearing a benign pheochromocytoma appears to be more than a simple coincidence, e.g., the incidence of thyroid cancer in such pts. is ten times greater than in the general population. (826 references)

- 64-1437 CELLULAR CONTROL MECHANISMS AND CANCER. (E.) Emmelot, P. (The Netherlands Cancer Institute, Amsterdam) and O. Mühlbock (Eds.). *Unio Internationalis Contra Cancrum Conference.* New York, Elsevier Publ. Co., 1964, 387 pp. illus. \$20.00.

Publication in book form of the papers presented by guests at the conference on 'Cellular Control Mechanisms and Cancer', held in Amsterdam, September 9-13, 1963. More than a dozen papers concerned with the general principles of the control mechanisms of cells, including mitosis, differentiation and inheritance, are followed by several papers on nucleotide metabolism, chromosomes in neoplasia, and biochemical studies of chemically induced hepatomas, growth of tumors in relation to the host, use of two-stage carcinogenesis as a tool for analysis of the nature of anticarcinogenic action as well as of leukemogenesis, and chemical and viral interactions in leukemogenesis; disappearance of an antigen or normal rat liver microsomes in experimental liver cancer, and interaction of carcinogens with proteins, nucleic acids and enzymes. The mechanisms of liver, mammary and epidermal carcinogenesis are reported in several papers. Viruses, particularly tumor viruses, and their mechanism of action are the subject of 5 papers and, in the final paper, some possible mechanisms of carcinogenesis are summarized. Also, discussions on genetic control of protein synthesis, growth regulation, structure and function of tumor cells and carcinogenic agents are reported. (500+ pertinent references)

- 64-1438 PATHOLOGY OF TUMOURS OF THE NERVOUS SYSTEM. (E.) Russell, D. S. (Bernhard

Baron Inst. Path., U. London), L. J. Rubinstein and C. E. Lumsden. Williams and Wilkins Co., Baltimore, Md., 1963, 343 pp. illus. \$13.50.

The second edition of an excellent monograph on the pathology of tumors of the nervous system includes a discussion of congenital tumors due to faulty development, and tumors of the various tissues and organs of the central and peripheral nervous system. Etiopathogenesis, including the genetic aspects of Lindau's syndrome, Recklinghausen's disease, tuberose sclerosis and some forms of neuro-cutaneous melanosis, is discussed. Some of the work on the production of neoplasms by the use of chemical carcinogens is reviewed. Also discussed briefly is the role of radiation, trauma and infections and parasites. (38 pertinent references)

- 64-1439 MOLECULAR PHARMACOLOGY. THE MODE OF ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS. VOL. I. (E.) Ariëns, E. J. (Ed.) (Dept. Pharmacol., U. Nijmegen, The Netherlands). Vol. 3-1 in Medicinal Chemistry. A Series of Monographs. De Stevens, G. (Ed.). Academic Press, New York, 1964, 503 pp., \$17.00.

An attempt to integrate current knowledge of interactions between living cells and drug molecules, including anticancer and carcinogenic agents, and to explain the action of drugs on living cells and organisms from a mechanistic point of view. Among topics discussed are problems of drug resistance, sensitization, tolerance, and receptor systems. (1000+ references)

- 64-1440 LUNG CANCER AND SMOKING. (E.) Editorial. Lancet 1:1374-1375, 1964.

In this editorial the author reviews two controversial interpretations of the relationship of lung cancer to smoking: that smoking is an established link in the causal chain (Doll and Hill, see CRA 2(8):#1563, and #1564, 1964) and that evidence admits of other quite different interpretations. T. W. Lees has proposed another explanation: that smoking is a habit of the healthy only, and that only the healthy succumb to "acute" diseases such as lung cancer (see CRA 2(6):#1159, 1964). Some of the objections to the latter hypothesis are presented. (8 references)

- 64-1441 LUNG CANCER AND SMOKING. (E.) Huddy, E. C. H. Lancet 2:313, 1964.

In a letter to the editor, the author objects to misleading statements on lung cancer incidence in pipe or cigar smokers. According to British and American statistics, it is shown that pipe smokers as a class have approx. 3x the probability on the av. of dying of lung cancer as nonsmokers. However, only in the U.S.A. were there enough

pure cigar smokers so that the lung cancer death rate could be estimated; this rate appeared to be the same as for nonsmokers. (3 references)

- 64-1442 IMMUNOLOGICAL ASPECTS OF CANCER. (E.) Woodruff, M. F. A. (Dept. Surg. Sci., U. Edinburgh, Scotland). Lancet 2:265-270, 1964.

This review which deals with non-endocrine factors in the immunologic control of cancer cites examples of tumor regression (conversely, sudden re-appearance after quiescence). Also discussed is immunogenetics of tumor transplantation, immunological properties of autochthonous tumors, and various aspects of the attempt to utilize immunologic reactions in cancer therapy. (86 references)

- 64-1443 CARCINOGENESIS RELATED TO FOODS CONTAMINATED BY PROCESSING AND FUNGAL METABOLITES. (E.) Kraybill, H. F. (Bur. Env. Health, U. S. Publ. Health Serv., Dept. Health, Educ., Welfare, Washington, D. C.) and M. B. Shimkin. Pp. 191-248 in Advances in Cancer Research. Vol. 8. Haddow, A. and S. Weinhouse (Eds.). Academic Press Inc., New York (Publ.), 482 pp., 1964.

A review of two major outbreaks of hepatoma in poultry and fish in different parts of the world. The hepatoma in trout occurred after the introduction on a large scale of some commercial feeds, composed of steam- or flame-dried fish or cottonseed meal or dried milk as the major source of protein. There is considerable evidence that the carcinogenic agent is contained in the lipid fraction and work is proceeding on the further characterization of the carcinogen. Work on the carcinogenic effect of various pesticides and other agricultural chemicals on fish is also reported. The hepatomas in poultry were found to be due to contamination by Aspergillus flavus of the peanut meal used in the feed. The crystalline carcinogenic agent, aflatoxin, has been shown to induce tumors in ducklings, turkeys, chickens, swine, cattle, horses and sheep. The carcinogenic properties of other fungal metabolites and associated compounds are reviewed as well as the relation between structure and carcinogenic activity. The health implications on a worldwide basis of the mycotoxicoses are discussed since there are wide variations in incidence of hepatomas, for example, which account for about 14% of all carcinomas in tropical areas of the Orient and Central Africa but less than 2.5% in the U. S. and Europe. A further striking example is the fact that moldy corn provides an important part of the African native diets. In male Bantus hepatomas represent 68% of all carcinomas. (110 references)

- 64-1444 THE EFFECTS OF ALKYLATING AGENTS ON FERTILITY. (E.) Jackson, H. (Dept. Exptl. Chemother., Christie Hosp., Manchester, England). Brit. Med. Bull. 20(2):107-114, 1964.

In a review and discussion of spermatogenesis and the antifertility effects of radiation and alkylating agents such as the aliphatic nitrogen mustards, ethyleneimines and methanesulfonic esters in the male rat, the author noted that stem-cell antifertility effects seem most relevant to the carcinogenic process, when an appropriate injury might result in the production of tumor cells. If this were true, busulfan, which appears to affect early spermatogonial stages, should be a carcinogen. However, if mutagenicity is the explanation of the antifertility effect on the later stages of spermatogenesis, then methyl methanesulfonate should also be an effective carcinogen. Very few of the antifertility agents have been tested for carcinogenicity. (32 references)

64-1445 PREVENTION OF CANCER. REPORT OF A WHO EXPERT COMMITTEE. (E.) Doll, W. R. S., Chairman (University Coll. Hosp. Sch. Med., London). WHO Tech. Rep. Ser. No. 276, 1964, 53 pp.

Report of the WHO committee of experts (other members include I. Berenblum, E. Caceres, W. Hueper, A. N. Novikov, H. Rahmatian and R. Truhaut) on prevention of cancer, defined as "elimination of, or protection against, factors known or believed to be involved in carcinogenesis and the treatment of precancerous conditions". After a discussion of general characteristics of carcinogenic agents, specific agents, including viruses, hormones and radiations, are discussed in an added section of the report. Precancerous lesions and their treatment are briefly described as are the etiological factors susceptible to control, such as exposure to sunlight, smoking, etc. The exposure to carcinogens in certain occupations, measures for their control, and the relation of the compensation laws to the carcinogenic hazard in industry are mentioned. The organization for cancer prevention and for examination of large populations is described. Other problems of control, such as legislation against proved industrial carcinogens, industrial hygiene, legislation requiring notification of occupational cancers, and education of physicians,

nurses, and others, as well as the general public, in cancer prevention are touched on briefly. A special program of education for general physicians, dentists and nurses, and a pilot scheme for cancer prevention in a town of 100,000 people are outlined. (29 references)

64-1446 EXPERIENCES WITH EXPERIMENTAL CHEMOTHERAPY OF VIRAL DISEASES. (E.)

Pienta, R. J. and V. Groupé. Pp. 525-586 in Experimental Chemotherapy. Vol. III. Part 2: Chemotherapy of Rickettsial and Viral Infections. Schnitzer, R. J. and F. Hawking. (Eds.). Academic Press, New York, 1964, 647 pp.

A short section of this extensive review is devoted to virus-host interactions (various aspects of the multiplication of viruses and reactions of the host to infection). Also discussed are the various test systems employed in viral chemotherapy, including tissue culture, embryonated egg and animal test systems. The animal test systems may employ either necrotizing viruses or oncogenic viruses, the latter group comprising Friend leukemia virus, Rous sarcoma virus, Moloney lymphoid leukemia virus and Rauscher leukemia virus. Various agents active against the leukemia or tumors induced by the above viruses are reviewed, along with their mode of action. (Approx. 288 references)

64-1447 THE DETERMINATION OF CARCINOGENIC ACTIVITY OF CHEMICAL SUBSTANCES. (E.)

Boyland, E. (Chester Beatty Res. Inst., London, S.W.3). Sci. Rep. Ist. Sup. Sanit. 2(4):439-444, 1962.

After reviewing some of the tests used to detect the carcinogenic activity of various chemical substances (food additives in particular), the author discusses some of the shortcomings and difficulties (time required for cancer induction, host susceptibility, effect of route and duration of admin.) encountered in this type of testing. (See also CRA 1(5):#826, 1963). (9 references)

See also abstract nos.: 1546, 1551, 1557, 1558

PHYSICAL CARCINOGENESIS

- 64-1448 PATHOLOGY OF SINGLE INTRAVENOUS DOSES OF POLONIUM. (E.) Casarett, G. W. (Dept. Radiat. Biol., U. Rochester Sch. Med., N. Y.). *Radiat. Res.* (Suppl. 5):246-321, 1964.

In a study of the effects of 1-20 $\mu\text{C/kg}$ single doses of polonium chloride (i.v.) in Wistar albino rats, incidence at 1 $\mu\text{C/kg}$, 5/40, was not significantly different from controls (3/34). In the treated rats tumors appeared from 420-570 days (controls 273-510 days). All 5 rats had pheochromocytomas, while 2/5 showed s.c. fibromas and 1/5 an epidermoid (squamous cell) carcinoma; 3 rats had 2 primary tumors each. In a series given 5 $\mu\text{C/kg}$, 13/42 revealed tumors (from day 246 to day 517) showing both increased incidence and usually earlier onset than in the 1 $\mu\text{C/kg}$ or control groups. Two of these rats had 2 primary tumors; another had 3 tumors. Malignant tumors included 1 spindle cell- and 3 reticulum cell sarcomas, 1 angiosarcoma (abdomen), 1 mammary carcinoma, 1 chronic myeloid leukemia, 2 renal carcinomas, 1 s.c. spindle cell sarcoma; incidence of benign tumors was about the same as in the 1 $\mu\text{C/kg}$ group. In the 10 $\mu\text{C/kg}$ series, 12/61 revealed tumors seen from 111-425 days. The data suggest an even earlier onset of tumors. Only 5/12 tumor-bearing rats possessed malignant tumors. One rat had 2 malignant primaries--gastric carcinoma and renal adenocarcinoma; other malignant tumors included 1 peritoneal endothelioma, 1 renal adenocarcinoma, 1 renal fibrosarcoma and 1 s.c. hemangioma. There were 10 benign tumors in 8 rats. Animals given 20 $\mu\text{C/kg}$ all died by day 160; 1 case of chronic myeloid leukemia was seen after 120 days.

- 64-1449 THE EFFECT OF LONG ULTRAVIOLET RADIATION ON THE DEVELOPMENT OF TUMORS INDUCED BY 20-METHYLCHOLANTHRENE. (E.) Clark, J. H. (Dept. Environ. Med., Johns Hopkins U. Sch. Hyg., Baltimore, Md.). *Cancer Res.* 24(2):207-211, 1964.

In Swiss albino mice exposed to a moderate dose of long UV radiation ($4-8 \times 10^7$ ergs/cm²) immediately after painting with 20-methylcholanthrene (MC; 2x/wk. for 12 wk.) the rate of papilloma development was accelerated but the rate of carcinoma development was unchanged. Prolonged UV ($10-18 \times 10^7$ ergs/cm²) was followed by an initial acceleration of papilloma growth, regressions and then an increase in rate so that final incidence was still less than that of controls. Carcinomas (which in controls first appeared at 105 days with a final incidence of 80%) developed slightly earlier (80 and 100 days, resp.) after UV 8.5 and 12.5×10^7 ergs/cm² and in fewer mice; after UV 18.4×10^7 ergs/cm², the first carcinoma appeared at 136 days and final incidence was only 30%.

- 64-1450 EXPOSURE TO ASBESTOS AND MESOTHELIOMA OF THE PLEURA. (E.) Fowler, P. B. S. (Charing Cross Hosp., England), J. C. Sloper and E. C. Warner. *Brit. Med. J.* 2:211-213, 1964.

"Asbestos bodies" were found in lung sections made at autopsy of 2 men with pleural mesotheliomas, aged 59 and 73, although neither pt. had developed severe pulmonary fibrosis. The younger pt. had a history of 16 yr. occupational exposure to inhalation of asbestos fiber, followed by 20 yr. without such exposure. The older pt. had been so exposed for a total of approx. 24 yr. prior to the onset of illness.

- 64-1451 TUMORS IN ALBINO RATS OF VARIOUS AGES AFTER A SINGLE ROENTGEN-IRRADIATION. (Ger.) Reincke, U. (Inst. Radiol., U. Freiburg i. Br., Germany), E. Stutz and G. Wegner. *Zschr. Krebsforsch.* 66(2):165-186, 1964.

A single total body irradiation (270 r) was given to male and female Wistar rats 5 days before birth or 13, 49 or 121 days after birth, and to gravid 121-day-old females. Among 512 surviving treated rats 402 tumors were diagnosed: 123, malignant; 3 "semi-malignant"; 276 benign. Among 118 controls there were 8 malignant and 36 benign tumors. Multiple tumors were found in a number of animals. Tumors were found in various organs except liver parenchyma, thyroid gland and the CNS. As to type they were carcinomas (adeno-, squamous cell, differentiated and non-differentiated); sarcomas (fibro-, polymorphocellular, spindle cell, lymphangio-, lympho-, reticular cell, etc.) and others with or without metastases. In contrast to the rate in controls, the frequency of malignant tumors in males was increased 6-10-fold, that in females 2-4 fold. This sex difference in treated rats was related chiefly to tumors of the genitalia. The female genital tumors increased significantly only after postnatal irradiation, and significantly decreased (probably due to hypoplasia of genital organs) after prenatal irradiation. Females irradiated during pregnancy showed fewer mammary tumors, than irradiated virgin rats. Of special interest is the fact that, in rats irradiated at the age of 13 days, a larger number of benign tumors were found; the number of ovarian tumors was also significantly increased. The authors conclude that no significant difference in the sensitivity toward carcinogenic radiation could be found at various ages. However, it seems that in reference to the formation of benign tumors in females there is some special sensitivity during the suckling period.

- 64-1452 INDIRECT TRANSFER OF RADIOGENIC LYMPHOMA. (E.) Ilbery, P. L. T. (U. Sydney, New S. Wales, Australia) and S. M. Winn. *Aust. J. Exp. Biol. Med. Sci.* 42(Pt. 1):133-148, 1964.

Following the inoc. of C57BL strain and (C57BL x T6/T6)F1 hybrid mice with the cell-free extract (CFE) of Co60-induced lymphoma, the following tumors were found in survivors: fibrosarcomas in 2/36, reticulum cell sarcomas in 2/36, lymphomas in 8/36. A median latent period of 600 days was seen, as compared to 200 days for the propositi following a leukemogenic schedule of irradiation. Karyotype studies showed that chromosome abnormalities in CFE-induced lymphomas were of the same high frequency as in radiogenic lymphomas. Cytogenetic examination of lymphomatous tissue from lymphomas in newborn mice following inoc. of CFE from radiation-induced lymphomas has not shown departure from the commonly noted counts of 40 - 1, 40 + 1, 40 + 2 and 0 + 3 previously seen in spontaneous lymphoma, radiogenic lymphoma and its preleukemic phase. A serious objection to a causal relationship between the observed chromosome changes and lymphoma induction is represented by the fact that 4/25 (16%) of the mice with radiation-induced lymphomas showed no deviation from the normal mouse chromosome complement. In 47 (C57BL x DBA)F1 hybrids oophorectomized between the age of 30-40 days followed by irradiation and subsequently treated with various tissue implants (thymus, spleen, liver and lung or brain), only 2 mice, both receiving thymic implants, developed a neoplasm at the site of implant.

1453 A HISTOPATHOLOGIC STUDY OF CARCINOMA OF THE UTERUS FOLLOWING IRRADIATION FOR DYSFUNCTIONAL UTERINE BLEEDING. (E.) Vakil, V. (Tata Mem. Hosp., Bombay, India) and M. V. Prasad. *Indian J. Med. Res.* 52(4):368-375, 1964.

pts. with uterine carcinomas (aged 50-62 yr.) have histories of previous induction of menopause by radiotherapy for abnormal uterine bleeding, menorrhagia or menstrual irregularity. In 3/4, the time intervals between irradiation and the discovery of cancer were 20, 10 and 10 yr.; in 1/4, the time interval and the radiation source were unknown. In 2/4, initial radiotherapy was by intracavitary radium, followed 1 and 7 yr. later, resp., by deep X-ray; in 1/4, it was by deep X-ray alone. Histopathologic changes in the uterine tissue are described in detail.

1454 PROLIFERATION OF THE TISSUE OF LYMPHOID ORGANS FOLLOWING IONIZING RADIATION. (S.) Mikhailov, V. P. (Inst. Exptl. Med., Acad. Sci. USSR, Leningrad), I. Georgiev and

Iu. Khussar. *Folia Med. (Plovdiv)* 6(2):71-75, 1964.

A report of some of the work presented on the effect of X-irradiation on the proliferation of lymph nodes, spleen and thymus. Mitotic index of thymic lymphocytes (L) in 3-week-old chicks decreased to a minimum in 24 hr., then increased to its max. on day 7. Aberrant mitoses reached their max. in the first 24 hr., then gradually decreased. Epithelial stroma and muscle fibers were replaced by those from the blood stream. This resulted in more or less normal mitotic activity and no increase of pathological mitoses in chicks receiving local irradiation of the neck. When the above organs of albino irradiated rats were transplanted into the abdomen of intact rats some L in the peripheral zone were able to divide and migrate, while others died in 24 hr. This resulted in a new growth of fibroblasts, polyblasts, L and giant multinucleated cells. In addition, splenic transplants (3 days old) had L-like cells but were rich in RNA and had basophilic cytoplasm. In another experiment it was shown that these transplants, being in contact with the recipient's cells in a chamber with a "capron" screen, were enriched by the latter so as to replace the dead and abnormal cells of the former.

64-1455 ISLAND-CELL TUMORS IN IRRADIATED RATS IN PARABIOSIS. (E.) Warren, S. (Cancer Res. Inst., New England Deaconess Hosp., Boston, Mass.), R. G. Carlstein, J. Steinke and R. N. Chute. *Proc. Soc. Exp. Biol. Med.* 115(4):910-912, 1964.

A supralethal single dose of 1000 r of whole body X-irradiation was given to the right-hand partner (the left-hand rat was shielded) of pairs of young inbred littermate Deac-Slonaker rats in parabiosis. Among 276 pairs of male to male parabionts, the incidence of adenoma and carcinoma, resp., of the islets of Langerhans in the unirradiated partners was 0.7% and 0%; in irradiated partners, 12% and 0.7%. Irradiated female parabionts (326 pairs) showed 2% adenoma and no carcinoma. The only tumor among parabiotic male and female controls was adenoma in 1% of the males. Insulin values (U/g wet wt.) for islet cell adenoma were 60-80 as compared with 1-3 in normal rat pancreas; however, studies of carbohydrate metabolism in a number of pairs failed to correlate with subsequent demonstration of insular adenomas. The predilection of islet cell tumors for male irradiated rats seems to correlate with the previously described higher frequency of diabetes in the male.

See also abstract nos.: 1425, 1426, 1431, 1445, 1513, 1594, 1601

CHEMICAL CARCINOGENESIS

64-1456 INACTIVITY AND TRANSFORMATION OF TRANSFORMING DNA WITH A CARCINOGENIC AGENT. (Jap., Abstract) Ono, T., Y. Iwamura and M. Ohashi. Seikagaku (J. Jap. Biochem. Soc.) 35(9):574, 1963.

The reaction between 4-nitroquinoline-N-oxide (4-NQO) or its reduced metabolite and transforming DNA was studied by the use of the transformation of the DNA of the hay bacillus as an indicator. 4-NQO, 2-methyl-4-NQO and 6-chloro-4-NQO had practically no effect, but the reduced metabolite of 4-NQO, that is, 4-hydroxyaminoquinoline-N-oxide (4-NHOHQO), had an inhibiting effect as strong as nitrogen mustard whereas the more reduced compound, 4-NH₂ base, and its metabolite without oxide, had no effect. The reaction between 4-NHOHQO and nucleic acid was not inhibited by a SH-base compound but was partially inhibited by acetone and hydroxylamine. No chemical change in base composition was found during reaction of the DNA of hay bacillus with 4-NHOHQO. There was no formation of reversible DNA as with nitrogen mustard, but lability of DNA was observed. 4-NHOHQO is considered to be the active form of 4-NQO.

64-1457 TWO CASES OF ENDOMETRIAL ADENOCARCINOMA RECEIVING EXCESSIVE ESTROGENS FOR LONG PERIODS OF TIME. (Jap.) Yamada, M. (Dept. Obstet. Gynec., Kyushu U. Sch. Med., Fukuoka, Japan) and H. Sugimori. Sanka To Fujinka (Obstet. Gynec. [Tokyo]) 30(3):345-349, 1963.

Two cases of endometrial adenocarcinoma, in Orientals, 36 and 67 yr. old, had histories of long-term treatment with estradiol (>25 x 10⁴ U in 17 yr., and >150 mg in 2 yr., resp.) because of hypoplasia of the uterus and ovarian deficiency syndrome, resp. Although it has not been proved, the authors suggest that long-term treatment with estradiol might play an important role in development or aggravation of carcinoma.

64-1458 CARCINOGENIC EFFECTS OF ZINC IN DRINKING WATER. (It.) De Szilvay, G. (Semmelweis Inst. Endocr., Bremen, Germany). Minerva Med. 55(38):1504-1505, 1964.

In a series of experiments, mice of unspecified strains (age and sex not specified) developed pulmonary adenomas and unspecified forms of uterine, mammary, bone marrow and other cancers after 5 or more mo. of ingesting drinking water to which 8-20 mg/l (in one group, up to 100 mg/l) zinc chloride had been added. The incidence of tumors in various experimental groups was as follows: 10/100 treated animals; 9/75, 4/50 also exposed to cigarette smoke; 16/100, 4/100 also exposed to cigar smoke. Tumor incidence in controls was, resp.: 0/40, 2/25, 2/50, not stated, 3/10. During a period of 3 yr. in which

4 generations of offspring of mice receiving up to 100 mg/l ZnCl in drinking water were subjected to the same regimen from birth, tumor incidence among the treated offspring rose to 30%, with tumor types including pulmonary adenomas, granulocellular tumors, leiomyomas, sarcomas and fibrosarcomas. The comparative incidence by tumor type is not indicated and no control group is reported. Animals not developing tumors increased zinc excretion as the conc. of admin. Zn was increased; those which developed tumors did not do so to the same extent. In a corollary study, the author found that drinking water from 8 cities in 3 different countries contained 8-50 mg/l zinc, although the maximal safe content is said to be 5 mg/l. In a further corollary study, he reports that persons in good health and with non-cancerous diseases eliminated 11.23-12.5 mg% over an unspecified period while cancer pts. eliminated only 4.88-5.42 mg%. He concludes that retention of zinc appears to be associated with carcinogenesis.

64-1459 INHALATION TOXICOLOGY OF OIL MISTS. I. CHRONIC EFFECTS OF WHITE MINERAL OIL. (E.) Wagner, W. D. (U.S. Dept. HEW, Div. Occup. Health, Cincinnati 2, Ohio), P. G. Wright and H. E. Stokinger. Med. Bull. Standard Oil Co. (N.J.) 24(2):135-152, 1964.

Inhalation of air containing petroleum base mineral oil mists (paraffins, 5.1%; non-condensed naphthenes, 27.0%; condensed naphthenes (2-6 rings), 67.9%) at levels of 5 or 100 mg/m³/day for 12-26 mo. by male mongrel dogs, Dutch rabbits, Golden Syrian hamsters, Holtzman-Sprague-Dawley rats, CF No. 1 mice and CAF₁/Jax mice did not produce any harmful effects at the lower dose. In CAF₁/Jax mice, 100 mg/m³ produced a slight increase in the number of tumors formed at 10-11 mo., but at 12-13 mo. the number of tumors was less than that of controls. Dogs inhaling 100 mg/m³/day for 26 mo. had parenchymal granulomas (containing lymphocytes, macrophages and free oil droplets) within the alveolar spaces or in close relation to the smaller bronchi and in hilar lymph nodes. Rats exposed to 100 mg/m³ had large numbers of lipid-filled macrophages in air spaces of the lungs. It was suggested that in the CAF₁/Jax mice the oil droplets were a "foreign body" insult.

64-1460 THE CARCINOGENICITY OF NONSAPONIFIABLE EXTRACTS FROM LIVERS OF SOUTH AFRICAN BANTU AND WHITE SUBJECTS. (E.) Higginson, J. (U. Kansas Med. Ctr., Kansas City), J. A. Dunn and D. A. Sutton. Exp. Molec. Path. 3(4): 297-303, 1964.

When nonsaponifiable extracts (NSE) obtained from livers of noncancerous white and Bantu subjects and from the livers of Bantu subjects with malignant hepatomas dissolved in chloroform were

Painted (3-10% conc.; 2x/wk. for 6 mo.) on the intrascapular region of 6-8-week-old Swiss mice of both sexes, no tumors were observed (except for 1 mammary adenocarcinoma which was probably incidental). Intrascapular s.c. inj. of the pooled NSE into Swiss mice resulted in the appearance of 8 fibrosarcomas (7/8 in females at 9-19 mo.; 1/8 in a male at 10 mo.); 2 of these were successfully transplanted into mice of the same strain. When female Hauschka mice were inj. s.c. with NSE the following results were seen: 4/6 spindle cell fibrosarcomas occurred in mice inj. with normal Bantü liver (vehicle sesame oil, S0, or tricapylin, T); 1/6 in mice inj. with normal white liver (S0 solvent); 1/6 in mice inj. with hepatoma liver (S0 solvent). Numerous typical mammary adenocarcinomas were observed in each group. Oleomas at the inj. site were more prominent and larger with S0 than with T. The cholesterol content and peroxide levels of the extracts used are also reported.

64-1461 INFLUENCE OF GONADAL HORMONES ON DMBA-INDUCED CARCINOMA OF THE CERVIX IN MICE. (E.) Meisels, A. (Dept. Path., Laval U., Quebec, Canada). *Acta Cytol.* (Baltimore) 8(4): 274-279, 1964.

The systemic admin. of testosterone (28 µg/inj./wk. in olive oil) to C3H mice bearing 9,10-dimethyl-12-benzanthracene-induced malignancies (mostly squamous cell carcinomas; 3 myosarcomas) of the uterine cervix decreased the latent period (LP) slightly (117.9 days as compared to 91.8 days in controls). On the other hand, α-estradiol (1 µg/wk. s.c.) increased the av. LP to 144.2 days. It is concluded that systemic admin. of estrogens can retard experimental carcinogenesis.

64-1462 THE INFLUENCE OF SEX HORMONES ON EXPERIMENTAL CARCINOMA OF THE UTERINE CERVIX IN MICE. (Fr.) Meisels, A. *Laval Med.* (4):422, 1964.

See CRA 2(8):#1461, 1964.

64-1463 THE STIMULATORY EFFECT OF 3-METHYLCHOLANTHRENE ON BENZPYRENE HYDROXYLASE ACTIVITY IN SEVERAL RAT TISSUES: INHIBITION BY ACTINOMYCIN D AND PUROMYCIN. (E.) Gelboin, H. V. (NIH, Bethesda) and N. R. Blackburn. *Cancer Res.* (2):356-360, 1964.

Normal male Sprague-Dawley rats were inj. i.p. with actinomycin D (AD; 19.8 µg) or puromycin (2.72 mg) 4 hr. before to 8 hr. after being inj. i.p. with 20-methylcholanthrene (MC). In tissue extracts prepared from the rats, it was found that MC alone caused a marked increase in the amount of benzpyrene hydroxylase (BPH) present in liver, small intestine, kidney and lungs; the level of enzyme was 10-100 times higher in the liver than in the other tissues. The MC-induced increase in BPH was inhibited 40-100% in the

tissues of animals treated with AD (an RNA synthesis inhibitor); AD was least effective as an inhibitor in lung tissue. In liver and intestine the inhibitory effect of P was greater than 90%, in kidney 37-90% and in lung 31-50%. The results indicate that the changes in BPH level are dependent on protein and RNA synthesis in the tissues. The possible relationship between genetic regulation of enzyme induction and carcinogenesis is discussed. (See also CRA 1(11):#1897, 1964.)

64-1464 LOCALIZING PROPERTIES OF ANTI-RAT HEPATOMA ANTIBODIES *IN VIVO*. (E.) Kyogoku, M. (Roswell Park Mem. Inst., Buffalo, N. Y.), Y. Yagi, J. Planinsek, J. Bernecky and D. Pressman. *Cancer Res.* 24(2):268-279, 1964.

The localizing properties of the antibodies against the stroma sediments of 2-acetylaminofluorene-induced hepatoma and normal liver were compared in tumor-bearing and normal rats using radioautography with ¹²⁵I-labeled antibodies and the fluorescent antibody technic. After inj. of globulin fractions of both antisera, antibody localized on the walls of sinusoids and in connective tissue parts of the tumor as well as in normal liver; localization properties of both sera were similar. After passage through normal rats (for 4 hr.), anti-hepatoma antibody localized preferentially in the connective tissue of the tumor, whereas the anti-normal liver antibody did not; neither serum localized on the walls of sinusoids. Apparently some components of the anti-sera were absorbed during circulation through a normal rat while other components were not absorbed from the anti-hepatoma serum.

64-1465 ANTIGENIC SPECIFICITY OF BENZO(a)PYRENE-INDUCED SARCOMAS. (E.) Globerson, A. (Weizmann Inst. Sci., Rehovoth, Israel) and M. Feldman. *J. Nat. Cancer Inst.* 32(6):1229-1243, 1964.

Sarcomas (fibro- or rhabdomyo-) induced in C3H and C57BL mice (both sexes; age 2-3 mo.) by 3,4-benzpyrene (BP) elicited isograft immune reactions to tumor-specific antigens. The antigenicity was highest in primary tumors and decreased gradually after serial transplantation in isologous hosts. Sarcomas that did not take in normal hosts grew progressively when transplanted to animals exposed to total body X-irradiation. The decreased antigenicity was not accompanied by complete loss of tumor antigens, since tumors that could no longer immunize animals were still susceptible to the immune response elicited by immunogenic grafts of earlier transplant generations. Distinct antigenic specificity was shown by each of the 2 sarcomas produced in a single animal by 2 simultaneous s.c. inj. of BP. Experiments in which sarcomas, originating in C3H and tested for antigenicity in (C3H x C57BL)F1 hybrids, showed that the lack of manifested immunologic reactivity to certain tumors is due to the properties of the tumor cells themselves and not to the recipient animals.

- 64-1466 ABORTIONS AND MALFORMATIONS UNDER THE INFLUENCE OF AN AGENT INDUCING HYPERLIPEMIA AND HYPERCHOLESTEREMIA. (Fr.) Tuchmann-Duplessis, H. (Dept. Embryol., U. Paris Sch. Med., Sorbonne) and A. Giroud. Bull. Acad. Nat. Med. (Paris) 148(19-20):392-398, 1964.

In an attempt to elucidate the mechanism underlying the frequency of gestational disturbances in pregnant diabetic women, transitory hyperlipemia and hypercholesteremia were induced by i.p. inj. of Triton W.R. 1339 into Swiss albino mice, Wistar rats, and a heterogeneous strain of rabbits. In mice, daily doses of 200-400 mg/kg (days 6-8 or 7-9 of pregnancy) slightly reduced the number of fetuses per litter, but had marked teratogenic effects. In rats, daily doses of 600-800 mg/kg x 2-3 between days 5-9 were required to produce similar results. In rabbits, at doses well tolerated by mouse or rat embryos, the agent was extremely embryotoxic; gestation proceeded only when the daily doses were reduced to 25-50 mg/kg for 2-6 days.

- 64-1467 SEVERAL OBSERVATIONS ON CIGARETTE SMOKE. (E.) Sato, T. (Dept. Nutr. Biochem., Inst. Public Health, Tokyo), T. Suzuki, J. Takayanagi and T. Okabe. Bull. Inst. Publ. Health 13(1):53-55, 1964.

When the freshly prepared condensate derived from the smoke of dried cigarettes was painted on the skin of 60 laboratory mice once a day, 5 days/wk., 2.5 yr. were required to induce the first tumor. Observations are also reported on labile free radicals in freshly prepared condensate determined by electron spin resonance.

- 64-1468 RESULTS OF COMPARATIVE DISTILLATION AND SMOKING TESTS OF TOBACCO. (Ger.) Kröller, E. (Dept. Food Chem., Max-von-Pettenkofer Inst., Berlin-Dahlem). Deutsch. Lebensmittellrundschr. 60(7):214-215, 1964.

Distillation of approx. 30 g of finely cut tobacco leaves and mechanical smoking of 35 cigarettes yielded essentially the same results upon chromatographic analysis of the resulting condensates. Demonstrated were essentially the same quantities of 3,4-benzpyrene, phenanthrenequinone, anthraquinone, phenol, m- and p-cresol and nicotine. Also demonstrated was the presence of 9,10-dimethyl-1,2-benzanthracene, 1,2,5,6-dibenzanthracene and 20-methylcholanthrene. The author concludes that distillation studies are reliable indicators of the potential dangers to health accruing from smoking tobacco products or tobacco substitutes.

- 64-1469 INDUCTION OF PULMONARY TUMOURS IN MICE BY NITROSONORNICOTINE, A POSSIBLE CONSTITUENT OF TOBACCO SMOKE. (E.) Boyland, E. (Chester Beatty Res. Inst., London, S.W.3),

- F. J. C. Roe and J. W. Gorrod. Nature (London) 202:1126, 1964.

When nitrosonornicotine (0.1 ml 2% soln. in arachis oil) was inj. i.p., 1x/wk. x 41, into 6 week-old, male and female, Chester Beatty mice, no tumors could be demonstrated in 25/40 animals which died during the first 7 mo. of treatment. Histologically confirmed, usually multiple, pulmonary adenomas were found in 7/8 which died after the beginning of the 8th mo.; a localized renal lymphosarcoma was found in 1/8. At the time of report, 7 additional treated animals were still surviving. Among controls receiving only arachis oil, 24/30 died during the first 7 mo., also without demonstrable tumors; 1/6 sacrificed during the 11th mo. had a pulmonary adenoma. Although no pulmonary tumors other than adenomas are reported among the animals treated with nitrosonornicotine, the authors conclude that this compound was a 'potent carcinogen for mouse lung'. He also states that efforts to demonstrate the presence of nitrosonornicotine and nitrosoanabasine in cigarette smoke have not been successful.

- 64-1470 THE BIOCHEMISTRY OF URETHANE. (E.) Boyland, E., R. Nery and K. Williams. Pp. 73-74 in British Empire Cancer Campaign 1963. Part 2: Scientific Report. British Empire Cancer Campaign Research. London, S.W.1, 707 pp., 1963.

See CRA 2(4):#670, 1964.

- 64-1471 SKIN TUMORIGENESIS BY 7,12-DIMETHYLBENZ(a)ANTHRACENE: INHIBITION BY ACTINOMYCIN D. (E.) Gelboin, H. V. (NCI, Bethesda) and M. Klein. Science 145:1321-1322, 1964.

Topical application to a group of 35 male Swiss mice of actinomycin D (A; 14 µg in 0.2 ml of acetone) 6 times, at 2, 5 and 8 hr. before and 2, 5 and 8 hr. after a single application of 9,10-dimethyl-1,2-benzanthracene (DMBA; 12 µg in 0.2 ml of acetone) followed by weekly topical applications of croton oil reduced tumor incidence by 82%. Groups of 35 acetone only controls had 1 mouse with 1 tumor; acetone + A controls had no tumors. Studies designed to detect a possible interaction between A and DMBA were negative. It is suggested that the early biochemical events of skin tumorigenesis by DMBA are dependent on the presence of genetic activity expressed in the form of DNA-directed RNA synthesis or in subsequent events.

- 64-1472 STUDIES ON SPONTANEOUS NEOPLASMS IN C3H/Fg MICE WITH PARTICULAR EMPHASIS ON LEUKEMIA. (E., Ph. D. Thesis, Order No. 63-5935, Univ. Microfilms, Inc., Ann Arbor, Mich.) Fuchs, P. C. (U. Maryland, Baltimore). Diss. Abstr. 24(3):1146, 1963.

Results of observation and autopsy studies on

spontaneous neoplasms in 238 stock non-breeding C3H/Fg mice (79 female, 159 male) showed the following incidence of spontaneous neoplasms: leukemia (mostly lymphocytic) 91%, mammary tumors 24% (females) and hepatoma 8% (males). In breeding females, mammary tumor incidence was 64% and leukemia incidence was 45%. Estrogen admin. suppressed leukemia development, but stimulated mammary tumor formation and inhibited hepatoma development. Gonadectomy increased the leukemia incidence in both sexes but inhibited mammary tumors and hepatomas. Adrenalectomy in females gave inconclusive results with leukemia, but partially suppressed mammary tumor development. The C3H/Fg leukemia was found to be easily transplanted, and a line was developed which now produces leukemia 1-2 wk. after inoc. In incomplete foster-nursing studies, a lower leukemia incidence was seen in C3H/Fg mice free of the milk agent. A significant reduction in leukemia incidence was seen in newborn and adult C3H/Fg mice inoc. with cell-free filtrates of C3H/Fg leukemic tissues or brains. Characteristic hepatic lesions and hypochromatic erythrocytes were observed with intracerebral inoc. of chick embryos with cell-free leukemic filtrates.

64-1473 PRELIMINARY SURVEY OF HYDROXYUREA (NSC-32065) AS A TERATOGEN. (E.)
Murphy, M. L. (Dept. Med., Cornell U. Coll. Med., New York) and S. Chaube. Cancer Chemother. Rep. (40):1-7, 1964.

In Wistar rats treated during pregnancy with single doses of hydroxyurea (HU; i.p. 500-2,000 mg/kg on day 9-12), fetal mortality was 100% and fetal abnormalities included stunted growth, encephaly, cleft palate, harelip, retarded and clubbed fore and rear appendages, and retarded tail. Urethan (U), hydroxyurethan and hydroxylamine produced no abnormalities in the fetal rat. Prior admin. of thymidine, guanine, adenine or citrovorum factor gave no protection. HU (inj. of 28-70 mg/egg) was more than 100 times more effective than U as a teratogenic agent in 4-day-old White Leghorn chick embryos; affected embryos generally did not survive to 18 days. In the sand dollar embryo, conc. of HU (20-500 µg/10 ml sea water) blocked development at the morula stage and numerous chromosome abnormalities were seen. HU-induced chromosome abnormalities, studied further in the sea urchin embryo, included anaphase lagging, polyploidy, fragmentation and some C-mitoses. U was found to inhibit cleavage only at 1000 times the conc. of HU; urea at the same dosage did not affect embryo development.

64-1474 CARCINOGENIC ACTIVITY OF A NEW ANTI-TUMOR AGENT, N-ISOPROPYL- α -(2-METHYLHYDRAZINO)-p-TOLUAMIDE, HYDROCHLORIDE (NSC-77213). (E.) Kelly, M. G. (NCI, Bethesda), R. W. O'Gara, S. Gadekar, S. T. Yancey and V. T. Oliverio. Cancer Chemother. Rep. (39):77-80, 1964.

Multiple pulmonary tumors (epithelial; similar to carcinogen-induced pulmonary adenocarcinomas) with an incidence of 100% appeared in adult CD2F₁ and General Purpose random-bred albino (GP) mice within 15 wk. after admin. of N-isopropyl- α -(2-methylhydrazino)-p-toluamide, hydrochloride (MIH) admin. i.p. (total 9-64 mg/mouse by single or repeated inj.) or p.o. (total 15-50 mg/mouse single or repeated). Tumors were seen in all mice given multiple inj. by 13 wk. after the start of treatment; with single high doses the latent period was longer and there were fewer tumor nodules/mouse. GP mice were more susceptible than CD2F₁ mice, as seen by the shorter latent period and higher nodule count. A 50% incidence of lymphocytic leukemia was seen in both CD2F₁ and GP mice following the same treatment schedule as above; the percentage was higher in mice receiving multiple inj. Mammary adenocarcinomas developed within 16 wk. after birth in 18% male and 100% female Osborne-Mendel rats given repeated admin. of MIH (total 40 mg/rat i.p. and p.o.).

64-1475 STUDY OF THE CARCINOGENIC EFFECT OF ISONICOTINIC ACID HYDRAZIDE (INH). (Jap.) Hashimoto, T. Kekkaku (Abstr. Current Lit. Tubercul.) 38(3):125-127, 1963.

INH was given to 28 dd female mice, 1.5-3.0 mg/day, p.o. or INHG (no details) for up to 12 mo. When 24 were sacrificed over a period of 2-12 mo. after start of treatment 11 lesions were found in the lungs; 2 were adenomas while the rest were hyperplastic foci. Distribution studies utilizing C14-labeled INH showed that distribution of INH in the lung showed no difference between normal lung tissues, adenomas or hyperplastic foci.

64-1476 ON THE ELECTRON MICROSCOPIC STRUCTURE OF A NEW TRANSPLANTABLE MOUSE ASCITES INDUCED BY ISONICOTINIC ACID HYDRAZIDE (INH). (Hun.) Kendrey, G. (Med. U. Budapest, Hungary) and L. Cossel. Magy. Onkol. 1(8):1-11, 1964.

A more extensive presentation of the paper abstracted as CRA 2(2):#228, 1964. Detailed data, including measurements, are presented of the ultrastructure of the INH-induced ascites tumor cells in the mouse. Some of the virus-like particles described were ring-shaped; the rim was 10-50 mµ in width while the inner area was approx. 16 mµ in diameter.

64-1477 EXPERIMENTAL STUDIES ON SYNCARCINOGENESIS. (Ger., Abstract) Schmähl Med. Welt 64(1):64-65, 1964.

See CRA 2(7):#1277, 1964.

64-1478 EXPERIMENTAL STUDIES ON MOUSE OVARIAN TUMORS INDUCED BY A SINGLE DOSE OF

7,12-DIMETHYLBENZ(d)ANTHRACENE. (Jap., Abstract) Morii, T. (Dept. Path., Kansai Coll. Med., Japan) and I. Kuwabara. Nippon Byori Gakkai Kaishi (Trans. Soc. Path. Jap.) 52:236-237, 1963.

The intragastric admin. of the compound indicated as 7,12-dimethylbenz(d)anthracene (DMBA; 10 mg in 0.5 ml sesame (teel) oil, s.c.) to 50-60 day-old virgin female C3H mice resulted in the induction of ovarian tumors (over 1 mm in diameter and 20 mg in wt.) in 13/22 mice after 7 mo. whereas none was observed in 25 controls 264 days after birth. Also, no tumors developed in 25 C57 black mice similarly treated with DMBA. Administration i.p. of 2.5 mg DMBA in 0.5 ml of an emulsion on days 45 and 65 after birth resulted in ovarian tumors in 5/14 surviving mice (C3H virgin females) 4 mo. after the first dose. Of this group, 65% had died of peritonitis within 2 mo. of the initial dose. The same dose of DMBA, injected once into the tail vein of 50-day-old C3H virgin female mice, caused ovarian tumors in 4/6 7 mo. after admin. Many mice died accidentally in these experiments. The ovarian tumors weighed 20-359 mg. Histologically, most were granulosa cell tumors. A few cases of mammary carcinoma, papilloma of the skin and adrenocortical tumors were also encountered.

64-1479 STUDY OF CARCINOGENESIS BY TISSUE CULTURE. (Jap.) Katsuta, H. (Res. Inst. Infect. Dis., U. Tokyo Sch. Med., Japan). Nippon Rinsho (Jap. J. Clin. Med.) 21(11): 2397-2401, 1963.

Minced liver tissue of F14-F16 albino JAR rats was cultured in roller tubes at 37°C, rotated 10x/hr., in a medium containing 20% cattle serum, 0.4% lactalbumin hydrate and salts, to which was added dimethylaminoazobenzene (DAB) in Tween 20, heated to 100°C followed by addition of salt solution, so that the final conc. in the medium was 1 µg/ml. The DAB was added daily for 4 days. Little proliferation of liver cells was noted in the controls whereas, in the cells of 15-20-day-old rats treated with DAB, there was a sudden, marked proliferation of small, round, parenchymatous liver cells, starting on day 12. In liver cells from rats over 1 mo. old DAB caused little proliferation. Inoculation of the proliferating cells into rats of the same strain (s.c., i.p., intraportally, or intrasplenically, or intracerebrally in 4-9-day-old rats) did not result in tumors. Malignancy was not induced in proliferating liver cells subcultured from the DAB-containing medium by the addition of the following agents to the medium; griseofulvin 1 µg/ml, α -naphthyl isothiocyanate 1 µg/ml, growth hormone 35 µg/ml, testosterone 1 or 10 µg/ml, or DAB 1 µg/ml/day x 4 added at 10- or 30-day intervals or 0.5 µg/ml/day added continuously during the period of observation.

64-1480 ACTIVATION AND DETOXIFICATION OF N-2-FLUORENYLACETAMIDE IN MAN. (E.)

Weisburger, J. H. (NCI, Bethesda), P. H. Grantham, E. Vanhorn, N. H. Steigbigel, D. P. Rall and E. K. Weisburger. Cancer Res. 24(3):475-479, 1964.

When a tracer dose (approx. 10 µC; 0.3 mg p.o.) of C14-labeled N-2-fluorenylacetamide was admin. to 5 male pts. (age 38-61 yr.) with various malignant diseases (lung carcinoma, mycosis fungoides, multiple myeloma, chronic myelogenous leukemia and teratocarcinoma of the testis), 46-74% was excreted within the first 12 hr. in the urine as an isotope. The principal detoxification product (24-30% of the dose) was a glucuronic acid conjugate, N-(7-hydroxy-2-fluorenyl)acetamide. The other major metabolite was N-hydroxy-2-fluorenylacetamide, a proximate carcinogenic product, representing from 4.4%-13% of the dose. Blood serum measurements indicated that the compound, as well as its metabolites, was in circulation only in small amounts at any one time. The livers of all pts. were functioning normally.

64-1481 DEPOSITION OF BENZO[a]PYRENE IN MOUSE FAT AFTER ORAL ADMINISTRATION. (E.)

Bock, F. G. (Roswell Park Mem. Inst., Buffalo, N. Y.), D. H. Smith and T. L. Dao. Cancer Res. 24(2):280-285, 1964.

The deposition of 3,4-benzpyrene (BP; p.o., 24 hr. before sacrifice) in abdominal adipose tissue of several strains of mice depended upon the type of solvent, conc. of BP in the test meal and genetic constitution of the test mouse. In 10 C57/St males, cholecystectomy one wk. prior did not change the amount of BP deposition in adipose tissue. In C57/St mice triolein was a less effective vehicle than olive (or sesame) oil whereas Tween 60 was more effective than olive oil; in 6 other strains Tween 60 and olive oil were equally effective. In C3H mice, BP at a conc. of 0.5-2.0% in a 0.2 ml vol. was followed by a positive correlation between dose and recovered BP, but BP at 1% in 0.05-0.4 ml produced max. deposition in fat at 0.15 ml and remained relatively constant with increased volumes. The 22 stocks of test mice were divisible into two groups: high level and low BP in the fat; the groupings tended to follow genetic relationships. In four strains BP deposition was significantly different for each sex, but this difference (as in the case of strain differences) may be a reflection of different body wt. (See also CRA 1(3):#396; *ibid.*, (7):1283, 1963; and *ibid.*, 2(1):#51, 1964.)

64-1482 4-NITROQUINOLINE N-OXIDE: AN INHIBITOR OF BENZPYRENE CARCINOGENESIS OF MOUSE SKIN. (E.) Searle, C. E. (Dept. Path., Birmingham Sch. Med., England) and D. L. Woodhouse. Cancer Res. 24(2):245-249, 1964.

The alternate application of 4-nitroquinoline N-oxide (NQO; 0.2 ml of 0.3% acetone soln. on day 1) and 3,4-benzpyrene (BP; 0.2 ml of 0.2% acetone soln. on day 4) to the mid-back skin of young, adult stock white mice caused a 4-week

delay in the appearance of the first skin papilloma and markedly reduced their subsequent rate of appearance. After 26 wk., only 27% had tumors compared to 80% in BP only controls. If these compounds were applied at separate sites, no inhibition resulted. Simultaneous weekly applications of the two again markedly reduced the incidence of tumors, but the mortality rate was greater than in controls. The same pattern of events occurred with simultaneous weekly applications of NQO and 1,2,5,6-dibenzanthracene (0.2 ml of 0.3% acetone soln.). The toxicity and possible mechanism of action of NQO are discussed. (See also CRA 1(7):#1279, 1963.)

64-1483 THE RESISTANCE OF TWO LINES OF RATS TO TUMOUR INDUCTION BY 3,4-BENZOPYRENE. (E.) Baudyšová, M. (Inst. Physiol., Czech. Acad. Sci., Prague), E. Holečková and B. Sekla. *Neoplasma* 11(3):293-298, 1964.

Among 48 Wistar rats of both sexes (approx. 200 g at the beginning of the experiment), tabulation was made of the percentages of animals bearing large, medium-sized, small and no tumors 4 mo. after s.c. inj. of 3,4-benzpyrene (BP; 3 mg in olive oil), as follows: 29.3, 12.5, 39.5 and 18.7, resp. Comparable tabulations for 48 bW rats of both sexes, under similar experimental conditions, were 10.2, 12.5, 45.8 and 31.5, resp.; for 20 bW females previously immunized by a single dose of 4.4×10^6 Walker 256 tumor cells in Tyrode soln., 5.0, 25.0, 20.0 and 50.0, resp. Minimal and max. survival times were, resp., 22 and 180 days, among 10/20 Wistar females; 23 and 200 days, among 10/20 non-immunized female blacks; 127 and 210 days, among 20/20 immunized female blacks. The authors conclude that a significant difference existed between the two strains, as concerned resistance to the carcinogenic activity of BP; that this difference was probably genetically determined and that it was further enhanced by previous immunization with another antigen.

64-1484 ESTROGEN-INDUCED KIDNEY TUMORS IN THE GOLDEN HAMSTER. II. DIETHYLSTILBESTROL ABSORPTION AND DISTRIBUTION IN TISSUES. (E.) Ward, D. N. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), J. D. Putsch, R. F. McGregor and P. Chang. *Cancer Res.* 24(2):319-327, 1964.

Male 6-16-week-old golden hamsters were implanted s.c. with diethylstilbestrol (DES) pellets (types B and C having densities of 0.70-0.76, 0.99-1.05 and 1.45 mg/mm³, resp.). Daily absorption varied from 150-630 µg DES/day with A > B > C; greatest absorption occurred in the 1st wk. then came fairly constant from wk. 3-8. Of hamsters continually bearing pellets which were renewed 3 times over a 7-8-mo. period, histologically confirmed renal carcinoma was noted in 5/6 with 6/7 with B and 6/7 with C; liver cysts occurred in 2/6, 1/7 and 2/7, resp. Gross

examination of animals bearing the pellets for 6 mo. showed 33% to have renal lesions which appeared to be tumors; in this group only 1 tumor was considered malignant; it was of the sarcoma type. Most lesions in the 6 and 7 mo. group were classed histologically as hyperplastic foci. The appearance of liver cysts did not appear to correlate with removal of DES after prolonged treatment as was indicated by previous experiments. There was no marked difference in the action of the 3 types of pellet.

64-1485 INCREASED INDUCTION OF SKIN TUMORS BY PRETREATMENT WITH CROTON OIL. (E.) Tannenbaum, A. (Michael Reese Hosp. Med. Ctr., Chicago, Ill.), S. D. Vesselinovitch and H. Silverstone. *Cancer Res.* 24(3):361-366, 1964.

The topical application of croton oil (CO; 0.02 ml of 0.15-1.0% soln. in acetone, total of 20-40 doses given twice weekly) to the interscapular skin of male and female (C57BL x C3H)F₁ mice or female DBA mice 2 wk. prior to treatment with 3,4-benzpyrene (BP; 0.02 ml of 0.2% in acetone, total of 10 doses, given twice weekly) resulted in a slight but significant increase in the incidence of skin tumors (from 6%-13%) and skin carcinomas (from 2%-8%). However, if treatment with CO followed that of BP, or was applied both before and after, a marked increase was seen (data for all groups combined): 50%-63% for skin tumors and 31%-51% for skin carcinomas. Acetone, applied alone, did not increase the incidence of tumors. These experiments indicate that CO possesses both mild carcinogenic activity and strong augmenting properties.

64-1486 THE EFFECT OF A CARCINOGEN (DMBA) APPLIED TO THE HAMSTER'S BUCCAL POUCH IN COMBINATION WITH CROTON OIL. (E.) Silberman, S. (Dept. Oral Path., Tufts U. Sch. Dent. Med., Boston, Mass.) and G. Shklar. *Oral Surg.* 16(11):1344-1355, 1963.

In male and female Syrian hamsters aged 2-3 mo., the addition of 1% croton oil to a 0.5% soln. of 9,10-dimethyl-1,2-benzanthracene (DMBA) in heavy mineral oil, applied to the buccal pouch 3x/wk., resulted in a greater degree of inflammatory infiltration and hyperkeratosis than that induced by application of DMBA alone to the contralateral pouch, and dyskeratosis developed more rapidly, although it failed to proceed to actual carcinoma as frequently. In general, the reverse situation was true in male and female animals aged 12-14 mo. and subjected to the same treatment.

64-1487 CHANGES IN THE ADENYLIC ACID DEAMINASE ACTIVITY OF RAT LIVER DURING CARCINOGENESIS. (E.) Kizer, D. E. (Samuel Roberts Noble Found., Inc., Ardmore, Okla.), C. A. Lovig, B. A. Howell and B. Cox. *Cancer Res.* 24(6):1050-1055, 1964.

When female Holtzman strain rats were fed the 3'-methyl-(3'-Me-) derivative of 4-dimethyl-aminoazobenzene (DAB) at a conc. of 0.06% in a semisynthetic basal diet for 12 wk., the hepatic adenylic acid deaminase (AMP) activity was elevated 1.5-2-fold from wk. 4-12. This elevation reversed 7-10 days after removal of the azo dye from the diet. With 4'-fluoro-DAB a similar elevation occurred, whereas 4'-Me-DAB or o-amino-azotoluene, both of which have low hepatic carcinogenic activity, did not alter the AMP activity. Yet, when rats fed 3'-Me-DAB were hypophysectomized or received a simultaneous feeding of the estrogenic compound p-hydroxypropiophenone (1.67% of diet), this elevation either did not occur or was greatly reduced. Feeding of α -naphthyl isothiocyanate caused transient early decrease in activity. Neither regeneration nor biliary proliferation produced this pattern of elevated AMP activity. Such a change, however, did occur with fasting and subsequent feeding of a low protein diet, indicating that elevated AMP activity is not exclusively characteristic of a precancerous liver.

- 64-1488 EFFECT OF AZO-DYE CARCINOGENESIS ON ENZYMES CONCERNED WITH UREA SYNTHESIS IN RAT LIVER. (E.) McLean, P. (Middlesex Hosp. Sch. Med., London, W.1), E. Reid and M. W. Gurney. *Biochem. J.* 91(3):464-473, 1964.

In a study of 4-dimethylaminoazobenzene (DAB) and some derivatives, when male albino rats (age 7 wk.) were fed a 20% protein diet containing 3'-methyl-DAB (3'-Me-DAB; 750 mg/kg diet) for 90-110 days, primary liver tumors arose within approx. 7-12 mo. The activity of all the urea cycle enzymes of these tumorous livers had markedly decreased. In tests made in precancerous liver, the urea cycle enzymes showed a particular pattern: transient increase in the activity of carbamoyl phosphate synthetase (CPS) after 5 days; increased arginase activity and a significantly decreased ornithine transcarbamoylase activity after 2 wk. After 6 wk. treatment with various carcinogenic azo dyes, a great decrease in the activity of all the urea cycle enzymes (CPS and ornithine transcarbamoylase in the mitochondria and arginine synthetase (AS), argininosuccinase and arginase in the soluble fraction of the cells) was seen, while those enzymes located in the soluble fraction decreased more slowly. Removal of the dye after 4 wk. of treatment resulted in a nearly complete reversal of the changes within 12 days. When rats were given 3'-Me-DAB for 2-5 wk., liver 6-phosphate dehydrogenase activity almost doubled while the activity of 6-phosphogluconate dehydrogenase remained unchanged. As compared to 3'-Me-DAB (600 mg/kg diet), the admin. of 4'-fluoro-DAB (600 mg/kg diet) produced a much greater effect after 6 wk., characterized by complete loss of activity of CPS and AS. Weakly or non-carcinogenic derivatives (4'-methyl-DAB or 2-methyl-DAB) did not cause significant decreases in these enzymes.

- 64-1489 THALIDOMIDE: EFFECTS ON ENZYMES OF GLUTAMIC ACID METABOLISM IN MICE. (E.) Hirschberg, E. (Dept. Biochem. Med., Columbia U. Coll. Physic. Surg., New York), M. Osnos, S. Bryant and J. E. Ultmann. *Science* 143:1343-1344, 1964.

Thalidomide (T), when inj. into mice or added *in vitro*, caused no significant alteration in the activity of glutamic decarboxylase in brain extracts or of glutamic dehydrogenase or glutamic oxalacetic transaminase in extracts of brain or liver. Lactic dehydrogenase also was unaffected by T *in vivo*. When Paris mice were given T, 250 mg/kg daily s.c. on days 6, 7, and 8 of pregnancy, extracts of the embryos and contiguous portions of the uterus 20 hr. after the last treatment showed no alterations in these enzyme activities.

- 64-1490 PREGNANCY DEPENDENCE OF MAMMARY TUMORS IN MOUSE SUBSTRAIN C3H/Cb/Se. (It.) Squartini, F. (Dept. Cancer Res., U. Perugia, Italy), E. Barola, I. Paoletti and G. Rossi. *Lav. Ist. Anat. Univ. Perugia* 24(1):29-37, 1964.

A study of the growth curves of 23 mammary tumors in C3H/Cb/Se female mice that delivered litters while bearing tumors (from among a total of 102 tumors in 151 mice) showed that 17.3% of the tumors were responsive to pregnancy, either totally (1/23; 4.3%) or partially (3/23; 13.0%) while 82.7% (19/23) failed to respond. These results differ from those obtained in RIII mice where the incidence of pregnancy dependent tumors was 80.3% and are close to those observed in BALB/Cf mice (19%).

- 64-1491 TUMOR-PROMOTING ACTIVITY OF EXTRACTS OF UNBURNED TOBACCO. (E.) Bock, F. G. (Roswell Park Mem. Inst., Buffalo, N. Y.), G. E. Moore and S. K. Crouch. *Science* 145:831-832, 1964.

During a period of observation of 36 wk., no tumors resulted when female ICR Swiss mice (aged 57 days at the start of the experiment) were given one topical application of 9,10-dimethyl-1,2-benzanthracene (DMBA; 125 μ g in 0.25 ml acetone), nor after applications of a conc. or a dilute, aqueous, Ba(OH)₂ extract (BE) or an acetone-benzene extract (ABEC) of unburned commercial cigarette tobacco (0.25 ml/day, 5 days/wk. for 9-36 wk.). However, when painting with the extracts was begun 21 days after pretreatment with DMBA as above, the dilute aqueous BE (approx. equivalent to the tobacco content of 0.5 cigarette/day) induced 11 small cutaneous papillomas in 2/30 mice; the conc. BE (equivalent to the tobacco content of 0.5 cigarette/day) induced 20 small cutaneous papillomas in 8/30 mice; the ABEC (equivalent to the tobacco content of 2 1/2 cigarettes/day) induced 16 tumors of the same sort in 7/30 mice. Some of the tumors regressed spontaneously in spite of continued treatment. The authors feel their study is significant in relation to the possible carcinogenic effect of chewing tobacco or mixtures of tobacco and lime; that it may also be significant in relation to the

question of cigarette smoking and lung cancer, since carcinogens other than those resulting from destructive distillation of cigarette components might be volatilized by pyrolysis and passed in the smoke.

64-1492 STUDIES ON MITOCHONDRIAL SWELLING AND ELECTRON TRANSPORT DURING NORMAL AND MALIGNANT TISSUE GROWTH. (E., Abstract) Gosch, H. H. Bull. Tulane Med. Fac. 23(4):292-293, 1964.

Rat liver mitochondria (M) isolated from tumors induced by 2 derivatives of dimethylaminoazobenzene (DAB; 4'-fluoro-DAB and 4'-ethyl-2-methyl-DAB), 2-acetylaminofluorene, ethionine and tannic acid were found to have a low level of swelling in all test systems studied, similar to that found in previous studies with 3'-methyl-DAB (3'-Me-DAB); azobenzene and 4-diethylaminoazobenzene had little effect. Hypophysectomy protected against the changes in M swelling during 3'-Me-DAB feeding. Partial hepatectomy (PH) and i.p. inj. of 20-methylcholanthrene caused a marked, but transitory, decrease of M swelling. The endogenous substance(s) which cause the decreased M swelling were found to be associated with the membrane and present in the M at high levels. The cocarcinogenic influence of PH did not alter resistance of the guinea pig to 3'-Me-DAB-induced tumors. The admin. of 3'-Me-DAB for 4 wk. caused denaturation of a fraction of the mitochondrial membrane sites which resulted in kinetic curves similar to those obtained in non-competitive enzyme inhibition. The changes in the rate of oxidation of DPNH paralleled the changes in swelling when during feeding of 3'-Me-DAB. No correlation was seen between the *in vitro* inhibition of substrate oxidation by M produced by 3'-Me-DAB, DAB and 2-Me-DAB and their resp. carcinogenic activity.

64-1493 EOSINOPHIL LEUCOCYTE REACTION TO TRICYCLOQUINAZOLINE-TREATED CELLS AND TO A CHEMICAL. (E.) Goswami, P. K. (Dept. Exptl. Med., U. Leeds Sch. Med., England). Nature (London) 202:1227-1228, 1964.

7/RCH mice (male, age 3-4 mo.), inoc. s.c. with liver cells derived from donors of the same strain which had received tricycloquinazoline (TCQ) in olive oil, i.p., 24-48 hr. before sacrifice, showed a local neutrophil leukocyte reaction 24-48 hr. after inoc. The reaction disappeared by day 3, followed by accumulation of eosinophils and small and large mononuclear cells. The number of eosinophils reached a peak on day 5, remained at this level until day 7, then declined rapidly until the s.c. tissue was normal by day 11. Injection of TCQ s.c. induced a similar, but prolonged reaction, with local infiltration increasing between wk. 1-3, plateauing at peak levels between wk. 3-4, and then declining slowly. Methylcholanthrene, inj. s.c., also resulted in local eosinophilia between day 30-90 after inj., although the reaction was less marked than that induced by TCQ. Carcinogenic effects were noted.

64-1494 TERATOGENIC EFFECTS OF THIAMINE DISULFIDE UPON THE OFFSPRING IN PREGNANT MICE. (Jap.) Endo, A. (Niigata U. Sch. Med., Japan) and M. Takahashi. Niigata Igakai Zasshi (Niigata Med. J.) 78(3):62-68, 1964.

64-1495 THE TERATOGENIC EFFECT OF THE STEROID NUCLEUS IN THE RAT. (E.) Buresh, J. J. (Creighton U. Sch. Dent., Omaha, Neb.) and T. J. Urban. J. Dent. Res. 43(4):548-554, 1964.

Treatment of 5 pregnant Snell-Supplee albino rats with cholesterol (15 mg/day, days 8 through 14) resulted in an incidence of 56.8% of abnormal palates in the offspring (av. litter size, 10) when sacrificed on day 18.

64-1496 CYTOGENETIC STUDY OF THE VIRAL AND DIMETHYLBENZANTHRACENE-INDUCED RAT LEUKEMIAS. (Rus.) Fichidzhian, B. S. (Inst. Exptl. Clin. Oncol., Acad. Med. Sci. USSR, Moscow), E. E. Pogosiants and E. L. Prigozhina. Vop. Onkol. 10(3):34-41, 1964.

Random bred female rats (2-month-old) received 9,10-dimethyl-1,2-benzanthracene (DMBA; 36 mg within 6 wk.). Newborn rats received hemocytoblastosis-reticulosis virus. Among neoplasms reported there were 6 leukemias which developed after approx. 3-5 mo., 10 mammary cancer, sebaceous parotid gland tumors in 3, simultaneous multiple mammary and sebaceous parotid gland tumors combined with leukemia in 2. Transplantation of leukemia succeeded in 3/6 cases (LK-1, LK-5, and LK-6). Primary leukemias developed 6.5-8.5 mo. after admin. of Mazurenko virus. DMBA-induced leukemias were heteroploid (super- or subdiploid) while virus-induced leukemias were superdiploid (1) and diploid (2). Every one of the rat leukemias studied (except those that were diploid) showed cytogenetic individuality; some contained characteristic marker chromosomes. (See also CRA 2(3):#452, 1964.)

64-1497 THE PHOTODYNAMIC ACTIVITY OF POLYCYCLIC HYDROCARBON CARCINOGENS. (E.) Epstein, S. S. Acta Un. Int. Cancr. 19:599-601, 1963.

64-1498 THE EFFECT OF METHYLCHOLANTHRENE ON RAT PROSTATE GLANDS GROWN IN NATURAL AND SEMI-DEFINED MEDIUM. (E.) Lasnitzki, I. (Strangeways Res. Lab., Cambridge, England). Cancer Res. 24(6):973-981, 1964.

In addition to the data presented in CRA 2(6):#1071, 1964, a significant increase in cell division was seen in explants of rat ventral prostate tissue grown in natural medium and treated with 20-methylcholanthrene (MC). After 10 and 14 days' exposure, mitosis was approx. 5x that of controls; after 17 days, it was 9x the control value. In explants transferred to normal medium after 10 days exposure to MC, mitosis was decreased. In

approx. 25% of the mitotic cells, various abnormalities (dislocation and clumping of chromosomes, diminution or complete absence of 50% of the chromosome complement in anaphase and dividing binucleate cells) could be distinguished. In the semi-defined medium, the effect of MC was much less marked and limited to an increase in cell size and formation of papillary projections.

64-1499 EARLY EFFECTS OF A SINGLE APPLICATION OF 3-METHYLCHOLANTHRENE IN BENZENE SOLUTION ON THE EPIDERMIS OF HAIRLESS MICE STUDIED BY MEANS OF A TETRAZOLIUM REDUCTION METHOD. (E.) Iversen, O. H. Acta Un. Int. Cancr. 19:602-604 1963.

See CRA 1(2):#243, 1963.

64-1500 THALIDOMIDE: EFFECTS ON EHRlich ASCITES TUMOR CELLS IN VITRO. (E.) DiPaolo, J. A. (NCI, Bethesda) and C. E. Wenner. Science 144(1):1583, 1964.

After 12 hr. exposure to thalidomide (T; 750 µg in 3 ml of fresh medium), Ehrlich carcinoma cells (ECC) showed 66.75 ± 8.2 mitotic figures/1,000 cells examined as compared to 34.45 ± 5.9 for unexposed ECC. At 24 hr. the control ECC showed the same incidence of mitotic figures as did the treated ECC at 12 hr. The increased rate of mitosis in T-treated ECC was not reversed by the addition (per ml of medium) of 10 µg nicotinic acid, folic acid or pyridoxal HCl nor by 2.5 µg of riboflavin. Discs of T (25-100 µg) did not inhibit dehydrogenase activity or growth of Ehrlich ascites tumor cells in agar. Oxygen uptake by the tumor cells was not affected by T.

64-1501 MEDIASTINAL LYMPHOMA IN SWISS MICE RECEIVING URETHAN. I. HISTOLOGIC STUDY. (Fr.) Driessens, J., A. Clay, J. Vanlerenberghe, L. Adenis and P. Quandalle. C. R. Soc. Biol. (Paris) 158(3):565-567, 1964.

Of 187 Gif-sur-Ivette mice (both sexes; av. wt. 25 g) given ethyl urethan (1% in the drinking water) for periods of 4-20 wk. or continuously until death, 81 (43%) developed mediastinal tumors some of which were accompanied by lesions of the spleen, liver and kidneys. The av. duration of the treatment in tumor-bearing mice was 19 wk. The av. latent period was 27 wk. (range 10-60 wk.). Microscopically, the tumors had the appearance of a lymphoblastic sarcoma; the same tumor cells were found in the spleen, liver and kidneys along with an infiltration of the leukemic type. Bone marrow presented either a complete lymphoid or lymphoblastic transformation. In

addition, all the animals presented pulmonary adenomas (see CRA 1(2):#233, 1963). A direct leukemogenic effect of urethan as well as the possibility of its unmasking a latent carcinogenic virus is considered.

64-1502 DETECTION OF CANCEROGENIC HYDROCARBONS WITH THE FINE STRUCTURE FLUORESCENT SPECTRA. (E.) Dikun, P. P. Acta Un. Int. Cancr. 19:484-485, 1963.

64-1503 ROLE OF CELL PROLIFERATION IN HEPATIC CARCINOGENESIS. (E.) Rubin, E. (Dept. Path., Mount Sinai Hosp., New York, N. Y.), K. Masuko, S. Goldfarb and F. G. Zak. Proc. Soc. Exp. Biol. Med. 115(2):381-384, 1964.

Primary hepatic carcinoma without accompanying cirrhosis or fibrosis of the liver was induced in 6 male Sprague-Dawley rats (av. wt. 150 g) given 0.005% diethylnitrosamine (approx. 1.5 mg/day) in their drinking water. The livers of these rats presented both hyperplastic nodules and nodular cytoplasmic alterations. Autoradiographs, after the admin. of tritiated thymidine, showed a considerable increase of DNA synthesis in both hyperplastic nodules and carcinoma, while no change was observed in morphologically normal areas or in foci of cytoplasmic alteration. These results indicate that primary hepatic carcinoma in the non-cirrhotic liver may arise through transitional stages involving increased nodular regeneration.

64-1504 MEASUREMENT OF POLYCYCLIC AROMATIC HYDROCARBONS IN THE AIR OF SYDNEY USING VERY LONG ALUMINA COLUMNS FOR SEPARATION. (E.) Cleary, G. J. Air Water Pollut. 7:753-767, 1963.

64-1505 DEOXYRIBONUCLEIC ACID POLYMERASE ACTIVITY DURING AZO DYE CARCINOGENESIS. (E.) Furlong, N. B. (Baylor U. Coll. Med., Houston, Texas) and A. J. Thomann. Proc. Soc. Exp. Biol. Med. 115(2):541-545, 1964.

Groups of male rats of the Holtzman strain (av. wt. 150-200 g) given 3'-methyl-4-dimethylaminoazobenzene (0.06% in the diet) were sacrificed at different times during the period of carcinogenic transformation of the liver (the first 8 wk. of dye-feeding) and the DNA polymerase activities in the soluble ultracentrifugal supernatant fraction of liver homogenates were measured. Enzyme values were doubled at 6 days, the earliest time at which activity was tested; this activity increased to almost 3 times the normal value through wk. 3 and then fell gradually toward values slightly above normal at the end of wk. 8.

See also abstract nos.: 1423, 1425, 1426, 1435, 1437, 1439, 1443, 1444, 1445, 1449, 1509, 1557, 1558, 1559, 1574, 1577, 1594

VIRAL CARCINOGENESIS

64-1506 EFFECT OF 5-iodo-2'-DEOXYURIDINE ON THE REPRODUCTION OF SV-40 IN TISSUE CULTURES. (Ger.) Haas, R. (Inst. Hygiene, U. Freiburg i. Br., Germany) and G. Maass. *Arch. Ges. Virusforsch.* 14(5):567-582, 1964.

Formation of SV40 virus, strain Vac/111/L (14.6.61) in the kidney tissue culture of *Cercopithecus aethiops* showed dose dependent inhibition by 5-iodo-2'-deoxyuridine (IUDR) added to the culture at 1-24 hr. (or even later) after infection with virus; during the initial virus adsorption period, however, IUDR did not interfere with viral multiplication. The IUDR interference can be reversed by the addition of thymidine. Virus synthesis was the same in tissues which had been grown in the presence of IUDR as in those grown in its absence.

64-1507 AUTOLOGOUS AND HOMOLOGOUS IMPLANTATION OF HUMAN CELLS TRANSFORMED IN VITRO BY SIMIAN VIRUS 40. (E.) Jensen, F. (Wistar Inst., Philadelphia, Pa.), H. Koprowski, J. S. Pagano, J. Pontén and R. G. Ravdin. *J. Nat. Cancer Inst.* 32(4):917-937, 1964.

Nodule formation following homologous and autologous implantation of simian virus 40 (SV40) transformed human cell cultures was observed in some pts. with terminal carcinomas of various organs (excluding infiltrative dermal neoplasms of extremities) who were inoc. with the transformed cells 1-31 days after chemotherapy was terminated (with the exception of 2 pts. who received cyclophosphamide on the day of implantation). No nodules were formed after homologous implantation of 5×10^6 cells from cultures during the early stages of the transformation process, whereas the same number of cells caused growth of nodules when obtained from late cultures. The homologous implantation of 5×10^6 HeLa cells usually caused nodules to form. Nodules brought out by HeLa and transformed cells eventually regressed, with the time required for regression somewhat greater for the HeLa cells. Experiments with homologous implants indicated that HeLa cells and late passage, virus-free SV40-transformed cells had a comparable neoplastic potential. Histologically, nodules produced by SV40-transformed human cells were sarcomas or possibly fibrosarcomas. Transformed cells could be recovered from biopsied nodules if they were cultured *in vitro*; reimplantation again produced nodules. Autologous implants (of transformed cells only) produced nodules in 2 pts. Reaction to re-exposure to autologous implants indicated that the cells may have acquired new antigenic properties. See also CRA 1(3):#480; *ibid.*, (5):#893; and *ibid.*, (8):#1560, 1963.)

64-1508 NEOPLASMS IN HAMSTERS INDUCED BY SIMIAN VIRUS 40. LIGHT AND ELECTRON

MICROSCOPIC OBSERVATIONS. (E.) Duffell, D. (Dept. Path., U. Minnesota Sch. Med., Minneapolis), R. Hinz and E. Nelson. *Am. J. Path.* 45(1):59-66, 1964.

Inoc. of SV40 (strain A 169F-3) into the left cerebral hemisphere induced intracerebral neoplasms in 9/27 Syrian hamsters less than 24 hr. old at the time of inoc.; extracerebral neoplasms in 3/27. The cerebral neoplasms, examined 90-126 days after inoc., were essentially papillary in nature, with vascular connective tissue cores and infiltration into adjacent cerebral parenchyma. Scattered foci of tumor cells were also found occasionally in other areas of the ventricular surface and in the subarachnoid space overlying the cerebellum and brain stem. CNS symptoms developed in only 4/9 animals. The extracerebral neoplasms, which appeared 127-247 days after inoc., were sarcomatous in nature and bore no morphologic relationship to the intracerebral tumors. Virus particles could not be demonstrated by electron microscopy in either group of tumors.

64-1509 THE NATURE OF THE HEMORRHAGIC LESIONS INDUCED BY POLYOMA VIRUS IN HAMSTERS. (E.) Defendi, V. (Wistar Inst., Philadelphia, Pa.) and J. M. Lehman. *Cancer Res.* 24(2):329-355, 1964.

Hemorrhagic lesions of the liver and lungs induced by polyoma virus (PV) in newborn and adult golden hamsters are discussed and microscopically analyzed. Animals with hemorrhagic lesions in the liver frequently had hemorrhagic lesions of the lung, but in all cases of such pulmonary lesions there were also the liver lesions. Nine out of 22 liver hemangioendotheliomas (8 from young hamsters and 1 from an adult) were successfully transplanted into unconditioned adults as were 5/12 pulmonary lesions. Some transplant lines gave a high incidence of metastases. Filtrates from hemangiosarcomas inoc. s.c. into 25-day-old hamsters failed to produce any tumors during an observation period of 5 mo. Comparisons of PV-induced transplantable tumors and 4-dimethylaminoazobenzene-induced transplantable hemangiosarcoma showed some similarity to Kaposi's sarcoma in man.

64-1510 AN ELECTRON MICROSCOPIC STUDY OF SPONTANEOUS MAMMARY CARCINOMA IN AKR MICE. (E.) Hiraki, K. (Dept. Int. Med., Okayama U. Sch. Med., Japan), S. Irino, Z. Ota, I. Miyoshi, S. Suzuki and M. Sato. *Gann (Jap. J. Cancer Res.)* 55(3):245-249, 1964.

Two spontaneous type B mammary adenocarcinomas have been reported in AKR mice, a strain in which leukemia incidence is high and spontaneous mammary tumors are very rare. One of them has been maintained in serial cell grafts up to the tenth

transplant generation. Electron microscope studies have revealed the presence in these tumors of numerous A and B particles, similar in number, size and morphology to those observed in mammary tumors in other mouse strains. It is concluded that no correlation exists between the incidence of spontaneous mammary carcinoma and the number of virus particles observed.

- 64-1511 FATE OF THE C3H MAMMARY TUMOR AGENT IN MICE OF STRAINS C57BL, I, AND BALB/c. (E.) Andervont, H. B. (NCI, Bethesda). *J. Nat. Cancer Inst.* 32(5):1189-1198, 1964.

The mammary tumor (MT) agent was transmitted to mice of low-MT strains C57BL, I and BALB/c foster-nursed by mice of high-MT strain C3H. These were the only mice that ingested C3H milk. The occurrence of MT was observed in the offspring obtained by brother x sister mating of fostered C57BL and I strains and the F₁ hybrids obtained by mating of the above with the C3H strain. None of the C57BL mice developed MT. In the C57BL hybrids, tumor incidence in the fostered group and the first 4 generations was, resp., 13/13, 4/9, 2/13, 0/24 and 1/6; no other MT has been seen in 35 completed generations. In strain I, 3 fostered mice and 12/26 hybrids born to fostered mice developed MT; no further tumors were seen in up to 6 generations. Thus, the MT agent disappeared from, or became inactive in, strains C57BL and I within a few generations, confirming earlier findings with C57BL mice in which a line was established whose ancestors carried the agent. On the other hand, a high-MT line of mice was obtained from low-MT strain of BALB/c mice nursed on C3H mice. A high incidence of MT was seen for 59 generations (37 reported here), and there is no evidence that the C3H agent had decreased or increased in activity throughout the generations studied.

- 64-1512 IMMUNITY TO TRANSPLANTABLE TUMORS FOLLOWING VIRAL ONCOLYSIS. I. MECHANISM OF IMMUNITY TO EHRLICH ASCITES TUMOR. (E.) Lindenmann, J. (Dept. Microbiol., U. Florida Coll. Med., Gainesville). *J. Immun.* 92(6): 912-919, 1964.

In inbred A2G mice, the i.p. LD₅₀ for Ehrlich ascites carcinoma was approx. 10 cells/mouse. Postoncolytic immunity was evidenced in mice inoc. with WSA strain of influenza A virus 4-6 days after inoc. of 10⁶ tumor cells. The mice were resistant to challenge 3 wk.-4 mo. later with 10⁶-10⁷ tumor cells. Resistance was induced in normal A2G mice by the adoptive transfer of 5 x 10⁶-5 x 10⁷ spleen cells or with plasma, serum or ascitic fluid from immune mice. However, random bred Swiss ICR mice could not be immunized by postoncolytic Ehrlich carcinoma immune sera from A2G mice. Agglutination of tumor cells *in vitro* occurred with sera which were protective *in vivo*. After fractionation of

the hyperimmune serum, it was found that the various fractions had *in vitro* agglutinin titers which were comparable to their *in vivo* protective ability; the antibodies concerned seemed to be associated with 7 S γ -globulin.

- 64-1513 THE EFFECT OF RADIATION ON SPLENO-MEGALY INDUCED BY THE FRIEND LEUKEMIA VIRUS AND ITS MODIFICATION BY ETHYL-N-bis(2,2-DIMETHYL-ETHYLAMIDINOPHOSPHORO)-CARBAMATE (AB-132), ACTINOMYCIN D, AND AET. (E.) Regelson, W. (Roswell Park Mem. Inst., Buffalo, N. Y.) and O. Pierucci. *Radiat. Res.* 22(2):368-382, 1964.

A new biological indicator of radiation damage is proposed which is based on using Friend leukemia virus-induced splenomegaly as the parameter. Groups of male Ha/ICR Swiss mice were admin. whole-body X-irradiation (X) 30 min. before or after AB-132 (500 mg i.p.); animals given AB-132 before X showed no survival 13 days later, but survival was 40% in animals given AB-132 after X as compared to 70% in the controls. In normal mice and mice infected 24 hr. previously with Friend leukemia virus, a combination of AB-132 + X reduced splenic wt. to a greater extent than each one alone; the potentiation effect was max. at day 6 after virus inoc. and was still marked at day 12 but was absent thereafter. An independent action was seen for actinomycin D + X, while radioprotective action occurred with aminoethylisothiourrea dihydrobromide when given prior to X, but not when given after X.

- 64-1514 STUDIES ON INDUCED RESISTANCE AGAINST ISOTRANSPLANTS OF VIRUS-INDUCED LEUKEMIA. (E.) Glynn, J. P. (NCI, Bethesda), A. R. Bianco and A. Goldin. *Cancer Res.* 24(3):502-508, 1964.

When male CDBA mice were pretreated with i.p. inj. of irradiated Moloney virus-induced (MLV) transplantable leukemia cells (11 inj. at 3-4 day intervals; total 2.5 x 10⁸ MCAS-10 cells), resistance was induced against an isologous s.c. MLV tumor transplant. Resistance was also induced by pretreatment with irradiated MLV cells (5 i.p. inj. at 3-4 day intervals; total 7.1 x 10⁷ LSTR-A cells) from an isologous transplantable tumor. The resistance developed by pretreatment with X-irradiated tumor suspensions of MLV-induced leukemias did not inhibit the growth of a leukemia induced by Rauscher virus. When male CDBA mice received total body irradiation 1 hr. prior to s.c. inoc. of MCAS-10 cells, the growth of the tumor was enhanced, particularly at a low inoculum conc. In BALB/c mice infected with MLV, transient interference with the growth of an isologous MLV-induced leukemia was observed.

- 64-1515 STUDIES ON ADAPTATION OF ROUS SARCOMA VIRUS TO DUCKS. (E.) Kuwata, T. (Dept. Bacteriol., Chiba U. Sch. Med., Japan). *Cancer Res.* 24(6):947-955, 1964.

Chick embryo suspension mixed with Rous sarcoma virus (RSV) was inoc. into 1-day-old ducklings and conditioned Golden hamsters. In hamsters, tumors grew which, though small, had a high virus titer. Temporary tumor growth followed by rapid regression was seen in ducklings. High doses of cortisone (C; 50 mg) were found to enhance tumor growth in ducklings infected with high titer virus. Examination of a tumor extirpated on day 7 from a C-treated duckling showed a chicken-type structure; extracts from this tumor induced sarcoma in chickens, but not in ducklings. However, once passed through conditioned hamsters, together with normal chick embryo, a duck-adapted variant virus was isolated. Duck-adapted RSV was able to induce tumors in both ducklings and chickens, even after passages in both birds.

64-1516 ASSAYS OF SUSCEPTIBILITY TO CHICK SARCOMA VIRUSES USING CHICK EMBRYOS OF SEVERAL BREEDS. (E.) Smidová, V. (Inst. Oncol. Res., Bratislava, Czech.) and B. Rada. Neoplasma 11(3):317-319, 1964.

Five strains of White Leghorn and 2 strains of New Hampshire chick embryos showed considerable variation in terms of sensitivity to inoc. of cell-free preparations of the Praha strain of Rous sarcoma virus on the chorioallantoic membrane (pock assay method), as well as considerable variation in the characteristics of chick embryo cell cultures infected with the same preparation. No response was seen in Cornish and Plymouth chick embryos. When an assay of 10⁻¹-10⁻⁶ dilutions of a cell-free preparation of B 77 myxosarcoma virus inoc. on the chorioallantoic membranes of White Leghorn chick embryos was compared with the induction of tumor takes in 1-day-old chicks of the same strain inoc. with the same materials, the susceptibility of the membrane proved to be less than the susceptibility of the chicks. The authors suggest that this phenomenon may be due to some unidentified factor or inhibitor which is present in the membrane.

64-1517 POCK FORMATION IN THE CHORIOALLANTOIC MEMBRANES OF DUCK EMBRYO INDUCED BY CHICK TUMOR VIRUSES. (E.) Smidová, V. (Inst. Oncol. Res., Bratislava, Czech.) and V. Thurzo. Neoplasma 11(3):320-323, 1964.

Inoc. of the chorioallantoic membranes of White Leghorn duck embryos with preparations of B 77 myxosarcoma virus, Praha strain Rous Sarcoma virus (RSV), or Fujinami chick tumor virus resulted in positive pock counts; a previous study showed all virus induced tumors in 1-day-old ducks. However, Bryan strain RSV, which did not induce successful tumor takes in young ducks in a previous experiment, also failed to yield a positive pock count in the present study. The authors conclude that duck chorioallantoic membrane can be used successfully as a test system with respect to the ability of a particular strain of chick tumor virus to induce tumors in young ducks.

64-1518 COMPLEMENT-FIXING ANTIGENS IN TISSUE CULTURES OF AVIAN LEUCOSIS VIRUSES.

(E.) Armstrong, D. (NCI, Bethesda), M. Okuyan and R. J. Huebner. Science 144(1):1584, 1964.

The complement-fixing (CF) antigens shared by 3 avian leukosis virus strains (erythroblastosis, RPL 12 and RIF) and the Schmidt-Ruppin (SR) sarcoma virus strain (as seen in CRA 2(5):#940, 1964) were found to be largely soluble, having failed to sediment when centrifuged at 30,000 RPM (59,364g) for 70 min. The uncentrifuged original virus preparation and the supernatant portions obtained after centrifugation were then titrated as antigens in the CF test with 8-16 U of hamster serum antibody to the SR virus. Results show that the original CF antigens were retained in all of the fractions, except in the pellets where they were reduced at least tenfold. Sedimented particles, presumably virus particles, contained the common sarcoma-leukosis antigen as well.

64-1519 TRANSFORMATION IN BONE MARROW CULTURES FROM LEUKEMIC AND NONLEUKEMIC CHILDREN. (Rum.) Benyesh-Melnick, M. (Dept. Virol. Epidemiol., Baylor U. Coll. Med., Houston, Texas). Stud. Cercet. Inframicrobiol. 15(2):109-114, 1964.

See CRA 1(8):#1580, 1963.

64-1520 ACUTE LEUKEMIA IN A 5-MONTH-OLD BABY GIRL BORN OF A MOTHER PRESENTING ACUTE LEUKEMIA AT THE TIME OF DELIVERY. (Fr.) Bernard, J. (Saint Louis Hosp., Paris), C. Jacquillat, F. Chavelet, M. Boiron, Y. Stoitchkov and J. Tanzer. Nouv. Rev. Franc. Hemat. 4(1):140-146, 1964.

A diagnosis of acute lymphoblastic leukemia was made in a 19-year-old pregnant woman on the day of delivery. Despite treatment the pt. died 5 mo. after diagnosis. The same diagnosis was made at the age of approx. 5 mo. in her daughter. Bone marrow karyotype studies (before treatment) of 15 mitoses (not in perfect condition) from 50 of the child's metaphases showed normal karyotype for the one 46-chromosome cell and a small acrocentric extra chromosomes, 46 of which were normal.

64-1521 TESTS IN HAMSTERS FOR ONCOGENIC QUALITY OF ORDINARY VIRUSES INCLUDING ADENOVIRUS TYPE 7. (E.) Girardi, A. J. (Merck Inst. Therap. Res., West Point, Pa.), M. R. Hilleman and R. E. Zwick. Proc. Soc. Exp. Biol. Med. 115(4):1141-1150, 1964.

The s.c., intrathoracic or i.p. admin. of various potentially oncogenic viruses to newborn hamsters resulted in the development of 61 malignancies (appearance ranging from 26-292 days) in 1,434 animals which survived weaning. The following tumors were seen in weaned animals: fibrosarcoma with adenovirus (AD) 2 (1/15); this culture was contaminated with SV40 and 1/11

control animals developed a liposarcoma. Other tumors included undifferentiated sarcomas with AD 7 (4/51); undifferentiated sarcomas with AD 12 (42/57); undifferentiated sarcomas with AD 18 (8/25); leiomyosarcoma with respiratory syncytial (myxovirus) virus (1/18); osteogenic sarcoma (1/15) and malignant lymphoma (probably a reticulum cell sarcoma) (1/15) with Rous sarcoma virus. Other tumors in controls included adrenal cortical carcinoma in 1/65 measles controls and reticulum cell sarcoma in 1/30 rhinovirus 23 controls. In an addendum, the authors report an incidence of 7/60 tumors in newborn hamsters inoc. with the AD 7 Pickney virus and the appearance of palpable masses resembling tumors in newborn hamsters inoc. with AD 7 Grider and Champagne types.

64-1522 PERSISTENT INFECTION OF HUMAN CELLS (HeLa) WITH ADENOVIRUS TYPE 12. (E.)

Van Hoosier, G. L., Jr. (Div. Exptl. Biol., Baylor U. Coll. Med., Houston, Texas), C. Gist, G. Taylor and J. J. Trentin. Proc. Soc. Exp. Biol. Med. 115(3):591-595, 1964.

In studies on the effect of different serum components on the titer of adenovirus Type 12 (A-12; Strain Huie) in HeLa cells, a delay in adenovirus cytopathic effect (CPE) and a reduction in final titer was observed with horse serum, calf serum and human serum as compared to agamma calf serum. An A-12 cell carrier system was established with the following characteristics: initial dependence on inhibitor or antibody in human serum, increased growth rate after day 5 as compared to uninfected cells, a high percentage of infected cells but relatively low percentage of detectable virus-yielding cells, and relative resistance to superinfection. No significant differences were noted in CPE using lower conc. of human serum or tryptose phosphate broth. No clones were observed with infected cells.

64-1523 IN VITRO TRANSFORMATION OF HAMSTER KIDNEY CELLS BY HUMAN ADENOVIRUS TYPE 12. (E.) McBride, W. D. Dept. Virol., California State Dept. Public Health, Berkeley) and A. Wiener. Proc. Soc. Exp. Biol. Med. 115(4): 870-874, 1964.

The *in vitro* transformation by human adenovirus Type 12 was obtained in the following types of kidney cell cultures derived from newborn hamsters: trypsinized cells, tissue fragments in plasma clots and tissue fragments separated from the culture medium by a continuous cellophane membrane. The transformation included morphological cell alteration, recovery of the ability to divide and development of an adenovirus Type 12 specific complement-fixing antigen without the presence of detectable infectious virus. No reaction was evident between the transformed cells and SV40 specific fluorescein tagged antibodies.

64-1524 THE CHROMOSOMES OF TUMORS INDUCED IN MICE BY HUMAN ADENOVIRUS, TYPE 12. (E.) Fjelde, A. (Dept. Exptl. Biol., Baylor U. Coll. Med., Houston, Texas), J. J. Trentin and E. Bryan. Proc. Soc. Exp. Biol. Med. 116(4):1102-1105, 1964.

When chromosome studies were done on four primary tumors in C3HfGs mice and 71 passage tumors induced in mice by human adenovirus Type 12, among 2001 cells analyzed, 56% presented the normal stemline (40 telocentrics) and 80% were in the diploid range (30-50). Aneuploidy, polyploidy, mixoploidy, and low rates of endoploidy were also seen. Structural aberrations were few (17/804) and consisted of metacentrics, breaks, rejoining constrictions, rings and extra long and minute chromosomes.

64-1525 CULTIVATION AND CHARACTERIZATION OF CELLS FROM A MALIGNANT LYMPHOMA IN AN AFRICAN CHILD. (E.) Fogh, J. (Sloan-Kettering Inst., Cornell U. Coll. Med., New York, N. Y.); H. C. Anderson, B. Allen, G. Petursson, E. L. Saunders and G. Dalldorf. Cancer Res. 24(3): 416-431, 1964.

Cells taken from a malignant lymphoma of the maxilla in an 8-year-old African male were cultivated and found to retain their morphologic characteristics after 15 mo. of serial passage: most dividing cells were diploid (yet the appearance of the interphase nuclei suggested higher chromosome numbers); the presence of considerable cytoplasmic activity with possible phagocytic properties; presence of lysosomes and micronuclei. These cultivated cells most closely resembled histiocytes, whereas the tumor cells in the malignant lymphoma resembled lymphoblasts. When cultivated cells (approx. 1×10^6 ; from passage 14) were inoc. s.c. into newborn Syrian hamsters or inoc. s.c. ($1-2 \times 10^6$ cells of passage 12, 16 and 18) into 3 cancer pts., no tumors developed. In addition, no positive results were obtained by inoc. of chicken chorioallantoic membrane or various types of tissue cultures with either lymphoma culture supernatant or supernatants from "blind passages" in the other type of cells. (See also CRA 2(4):#723, 1964.)

64-1526 CLINICAL FEATURES OF CONGENITAL LEUKEMIA. (Jap., Abstract) Arakawa, M. (Dept. Pediat., Tohoku U. Sch. Med., Japan). Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.) 26(5): 623, 1963.

A case is presented of a 28-day-old Oriental baby who developed skin ulcer with infiltration in whom a diagnosis of congenital leukemia was made. Both maternal and paternal grandfathers had carcinoma of the stomach; the parents were cousins. Three siblings, who died in infancy at almost the same age as the pt., experienced hemorrhages; they were also suspected of suffering from congenital leukemia.

64-1527 A STUDY OF RABBIT ANTIBODY AGAINST ROUS SARCOMA VIRUS. (E.) Fink, M. A. (NCI, Bethesda). *Proc. Soc. Exp. Biol. Med.* 115(3): 580-584, 1964.

An antiserum against Rous sarcoma virus (RSV) was prepared in 9-month-old rabbits receiving intra-abdominal inj. of 0.75 ml of a mixture of 1 part RSV and 2 parts Freund's adjuvant and 0.35 ml s.c. 3 wk. later of a similar preparation. The antiserum was found to contain large quantities of complement-fixing (CF) antibodies for RSV and high titers of neutralizing (N) antibody against RSV. After absorption of the antiserum with packed sheep erythrocytes (SRBC) and normal chicken tissues (liver and breast), the CF antibody reacting only with RSV remained, along with a large quantity of the N antibody. The addition of complement to the 1:100 dilution of anti-RSV serum, which had been absorbed with SRBC and chicken tissue, increased the neutralization index by 1.42 logs (from 2.42 to 3.85), indicating some enhancement of neutralization. These findings show that RSV antibody prepared in the rabbit is capable of fixing complement with RSV and that the antibody neutralizing RSV is directed against viral and not against normal tissue antigens.

64-1528 STUDIES ON LEUKEMIA IN THE C₃Hf STRAIN OF MICE. III. RESULTS OF CELL-FREE TRANSMISSION. (E.) Miyoshi, I. (Dept. Med., Okayama U. Sch. Med., Japan). *Nippon Ketsueki Gakkai Zasshi (Acta Haemat. Jap.)* 26(5):549-558, 1963.

56 newborn C₃Hf mice inoc. s.c. with cell-free leukemic filtrates (LF; 0.1-0.2 ml from liver, spleen and mesenteric lymph nodes of mice bearing transplanted leukemia, generations 2-10), 1 male mouse (among 18 that survived more than 1 yr.) developed a mesenteric reticulum cell neoplasm Type B; Hodgkin's-like lesion) at age 16 mo., while the other 17 were free from malignancy. The inoc. of cell-free brain filtrates (0.5 ml i.p.) from mice bearing leukemia into 3-5-week-old 4Hf, C₃H/He/Mi and C₃H/He/Mi/Ky mice failed to induce leukemia within a 6-mo. observation period. Upon the i.p. implantation of pieces of the mesenteric Type B lymph node into 3.5-month-old syngeneic mice, palpable abdominal tumors were evident at 6 wk. The first generation transplant assumed the histologic picture of reticulum cell neoplasm Type A (reticulum cell sarcoma) rather than the original primary Type B neoplasm.

64-1529 FURTHER STUDIES ON SV40-INDUCED TRANSFORMATION IN HUMAN RENAL CELL CULTURES. EVENTUAL FAILURE OF SUBCULTIVATION DESPITE A CONTINUING HIGH RATE OF CELL DIVISION. (E.) Wein, H. M. (Child. Hosp. Med. Ctr., Boston, Mass.), J. F. Enders, L. Palmer and E. Grogan. *Proc. Soc. Exp. Biol. Med.* 115(3):618-621, 1964.

cept for a single apparent exception, human

kidney cells transformed by SV40 exhibited a changing morphology and an eventual failure to persist in serial subcultivation. The increasing rate of aberrant nuclear division is suggested as an immediate factor responsible for the declining growth rate.

64-1530 PLASMA ENZYMES ERYTHROPOIESIS AND R.E.S. FUNCTION IN MICE FOLLOWING INFECTION WITH AN LDH AGENT. (E.) Bailey, J. M. (Dept. Biochem., George Washington U. Sch. Med., Washington, D. C.), J. Clough and M. Stearman. *Proc. Soc. Exp. Biol. Med.* 115(3):642-646, 1964.

Upon infection of BALB/c mice with lactic dehydrogenase (LDH) agent (from CD/5 lymphoma) by means of i.p. inj. of 0.01 ml of infectious plasma, it was found that RBC are not the source of additional LDH in plasma. Of 9 enzymes tested, only LDH responded to LDH agent with a significant rise in plasma level reaching a max. (5x normal) in 5 days and lasting 15 days. During the first 24 hr. following infection, plasma levels of LDH, MDH, GOT, GPT and SODH fell rapidly; all except LDH returned slowly to normal pre-infection levels. Hematocrit levels were slightly lower in infected mice, while erythropoiesis was not directly affected by the LDH agent. Half life T_{25/50} of carbon particle clearance from the blood stream was approx. the same for infected (30 min.) and normal (28 min.) mice. (See also CRA 1(12):#2125, 1964.)

64-1531 TRANSPLANT IMMUNITY TO POLYOMA VIRUS INDUCED TUMORS. I. CORRELATIONS WITH BIOLOGICAL PROPERTIES OF VIRUS STRAINS. (E.) Hare, J. D. (Dept. Microbiol., U. Rochester Sch. Med., N. Y.). *Proc. Soc. Exp. Biol. Med.* 115(3): 805-810, 1964.

In addition to data already reported in CRA 1(5):#924, 1963, it was found that simultaneous infection of hamsters with 2 polyoma virus strains (SE3049-H⁺ and PV1P) and subsequent challenge with 9 x 10⁴ and 9 x 10³ HTC-3049-3 tumor cells on day 28 enhanced the growth of the inoc. tumor cells and increased the oncogenicity (6/6 tumor takes, 3/6 developed hepatic hemangioendotheliomas and an occasional solid peritoneal tumor) in the doubly infected group.

64-1532 INFECTIOUS AND ONCOGENIC EFFECT OF DNA EXTRACTED FROM CELLS INFECTED WITH POLYOMA VIRUS. (E.) Orth, G. (Dept. Virol., Pasteur Inst., Paris), P. Atanasiu, M. Boiron, J. P. Rebière and C. Paoletti. *Proc. Soc. Exp. Biol. Med.* 115(4):1090-1095, 1964.

Thirty-five newborn hamsters (age 2-4 days) were inj. s.c. (approx. 70 µg) or intracerebrally (15 µg) with DNA extracted from embryonic mouse cells (see also CRA 1(6):#1151, 1963) in tissue cultures collected 4-6 days after infection with polyoma virus (PV). On day 30, all 34

survivors had specific anti-PV antibodies with titers varying between 1,920-30,200. Tumors developed in 26/34 after 2-3 mo. Some tumors were in the s.c. tissue, but some were seen also in the lungs and liver in association with hemorrhagic disease; 3 were in the thorax. Histologically, the tumors were fibrosarcomas and angiosarcomas. Adult hamsters (age 40 days) were less sensitive: tumor incidence was less (5/17) and the latent period was longer (5-6 mo.); 11/17 had anti-PV antibodies. The same DNA preparations proved to be infectious for mouse kidney cell cultures. That these results were due to DNA rather than to residual intact PV was established by the negative results obtained both *in vivo* and *in vitro* in the control series in which use was made of DNA treated with DNase or of DNA originating from non-infected cells. The possibility that the appearance of infection and tumors following inoc. with viral DNA was due to latent polyoma infection or to contact with several original reactors was also ruled out.

- 64-1533 ENHANCEMENT OF ADENOVIRUS GROWTH IN AFRICAN GREEN MONKEY KIDNEY CELL CULTURES BY SV40. (E.) Rabson, A. S. (NCI, Bethesda), G. T. O'Connor, I. K. Berezsky and F. J. Paul. Proc. Soc. Exp. Biol. Med. 116(1):187-190, 1964.

When African green monkey kidney cell (AGMK) cultures were infected with adenovirus 12 alone, cytopathogenic effects were produced; however, after 72 hr., less than 1% of the cells contained adenovirus particles by electron microscopy and titrations showed no increase in virus. When AGMK cultures were infected with both adenovirus 12 and SV40 viruses, after 72 hr. adenovirus particles were found in 75% of the cells and there was an increase in virus by titration. SV40 virus also enhanced the growth of adenovirus 5 in AGMK cultures. The development of progressive adenovirus-type cytopathic changes at a time when no adenovirus particles were present in AGMK cell cultures infected with adenovirus alone suggests the formation of an incomplete virus; in the presence of SV40 the process would go to completion.

- 64-1534 ATTEMPTS TO INTERRUPT VIRUS TUMORIGENESIS BY IMMUNIZATION USING HOMOLOGOUS "BJORKLUND-TYPE" ANTIGEN. (E.) Goldner, H. (Merck Inst. Therapeut. Res., West Point, Pa.), A. J. Girardi and M. R. Hilleman. Proc. Soc. Exp. Biol. Med. 114(2):456-467, 1963.

"Bjorklund-type" lipoprotein tumor antigen (1 or 2 ml i.m. and/or s.c. in aqueous or mineral oil vehicle) was admin. to newborn hamsters after s.c. inj. into the interscapular area of SV40 (0.2 ml, titer 10^{-6} or $10^{-7}/0.2$ ml) or polyoma virus (0.1 ml, titer $10^{-5.5}/0.2$ ml) and before the appearance of the first tumors. A definite trend toward enhancement of rate of tumor occurrence resulting from vaccination was seen in both tumor systems. When adult hamsters were challenged s.c. with a trypsinized suspension of SV40 hamster tumor cell

culture or were implanted s.c. with pieces of fresh hamster polyoma tumor tissue, a generally shortened induction period, but no protection, was seen in the vaccinated animals. In tests for the antibody-inducing capacity of "Bjorklund type" SV40 hamster tissue antigens in hamsters, rabbits and guinea pigs, most of the rabbits and guinea pigs developed precipitating antibody against primary and transplanted SV40 hamster tumor antigen, but only the rabbit antisera reacted with the extract of normal hamster muscle and only the guinea pig sera reacted with the "Bjorklund-type" antigen. Sera from most of the animals were frankly cytotoxic or depressed the growth of normal hamster cells in cultures.

- 64-1535 GLOMERULOSCLEROSIS IN MICE WITH MYELOID LEUKEMIA. (E.) Gude, W. D. (Oak Ridge Natl. Lab., Tenn.), V. K. Jenkins, A. C. Upton and R. L. Tyndall. Proc. Soc. Exp. Biol. Med. 115(3):691-693, 1964.

In RF/Up strain mice bearing passaged myeloid leukemia, intercapillary glomerulosclerosis was evident regardless of whether the mice developed leukemia from inoc. with leukemic cells or subcellular materials. In mice with rapidly developing leukemia, the glomerular lesions were seen as early as 2 wk. following inoc. The glomerular lesions were indistinguishable histologically from those induced by irradiation or developing spontaneously in aging controls of the same strain.

- 64-1536 A SIMPLIFIED TISSUE CULTURE TUBE NEUTRALIZATION TEST FOR ROUS SARCOMA VIRUS ANTIBODIES. (E.) Sarma, P. S. (U. S. Public Health Serv., NIH, Bethesda), R. J. Huebner and D. Armstrong. Proc. Soc. Exp. Biol. Med. 115(2):481-486, 1964.

A simplified tube neutralization test for assay of Rous sarcoma virus and related avian leukosis viruses antibodies is described. The test appears to be suitable for differentiating serotypes and for surveys of naturally occurring antibodies against these viruses. In preliminary surveys for Rous sarcoma antibodies in sera of various species, it was found that most hens in 3 commercial flocks of laying chickens were positive for antibody; one of 3 hens without detectable antibodies was found to have Resistance Inducing Factor viremia. No antibodies were found in sera from 24 8-week-old turkeys, 24 Japanese quail, 6 barn pigeons, 2 ducks and one guinea fowl. Also negative were sera from 7 laboratory workers exposed to avian leukosis virus, 14 adults with leukemia, 7 adults without leukemia or other neoplasms and 11 children who had been inoc. 1 mo. before with live attenuated measles vaccine produced in chick embryos.

- 64-1537 THE MAMMARY TUMOR AGENT IN COMPLETELY MAMMECTOMIZED MICE. (E.) Dux, A. (The Netherlands Cancer Inst., Amsterdam) and O. Mühlbock. Proc. Soc. Exp. Biol. Med. 115(2):433-435, 1964.

In mammary tumor agent-free (female C3HF x male 020)F₁ hybrid mice transplanted with splenic tissue from completely mastectomized or intact donors that had been previously exposed to mammary tumor agent (MTA), the mammary tumor incidence was 91% and 96%, resp.; the av. tumor age was 322 and 321 days, resp. Controls not receiving splenic tissue failed to show mammary tumors. These results indicate that MTA persists and/or propagates in the mouse in the absence of mammary glands.

64-1538 SERUM ENZYME LEVELS IN LINES OF CHICKENS DIFFERING IN SUSCEPTIBILITY TO LEUCOSIS. (E.) Wilcox, F. H. (Dept. Poultry Sci., U. Maryland, College Park). Proc. Soc. Exp. Biol. Med. 116(1):222-225, 1964.

When the level of 10 enzymes (acid and alkaline phosphatases, amylase, cathepsin (C), alkaline and acid DNases, glutamic-oxalacetic transaminase, lactic dehydrogenase, leucine aminopeptidase and lipase) was measured in sera of 10-day-old female chickens from lines resistant and susceptible to leukosis, it was found that the level of C was 60% higher in the resistant than in the susceptible line. Similar results (increase of 60%) were also obtained at 4 wk. of age. No significant and repeatable differences were observed in the other enzymes.

64-1539 THE ROLE OF DEOXYRIBONUCLEIC ACID IN THE SYNTHESIS OF ROUS SARCOMA VIRUS. (E.) Bader, J. P. (NCI, Bethesda). Virology 2(4):462-468, 1964.

In studies to determine the role of DNA in the growth of Rous sarcoma virus (RSV), actinomycin (1 µg/ml) was found to inhibit both DNA synthesis and DNA-dependent RNA synthesis in chick embryo cells. Conc. of 3 µg/ml suppressed RSV synthesis within 4 hr. after addition and prior to any obvious change in the microscopic morphology of the cells. The growth of vesicular stomatitis virus was not inhibited. RSV growth was significantly decreased but not completely inhibited by 5-bromodeoxyuridine (BUDR; 1-100 µg/ml). Cells pretreated with BUDR could support the growth of RSV if BUDR was removed, but exposure of pretreated cells to additional BUDR led to a 10-fold inhibition of virus growth. Essentially nondividing cells were capable of supporting the growth of RSV, and virus production in

these cells was inhibited by additional BUDR. Inhibition of RSV growth by BUDR was reversible by thymidine (100 µg/ml). It is concluded that the growth of RSV requires the synthesis of a new DNA, and that the RSV particle may possibly contain a DNA moiety.

64-1540 ROUS SARCOMA IN CHINESE HAMSTERS. (E.) Ahlström, C. G. (Inst. Path., U. Lund, Sweden), R. Kato and A. Levan. Science 144(1):1232-1233, 1964.

Fifteen newborn Chinese hamsters (CH) were inj. s.c. with either pooled homogenized or a fresh suspension of Rous chicken sarcoma and tumors appeared at the inj. site within 2-8 wk. Microscopically, the tumors were mostly spindle cell or polymorphous sarcomas with numerous mitoses; one each of tumors resembling human giant-cell tumor, hemangiosarcoma and malignant angioendothelioma was also found. Transplantation of 1 of the tumors into the cheek pouch of adult CH treated with hydrocortisone (H; 0.25 mg s.c.) was followed by the development of a small tumor, which rapidly regressed. Transplantation into the cheek pouches of 14 young Syrian hamsters (some of which were H-treated) resulted in the appearance of 2 tumors in H-treated animals and 2 in untreated animals which grew very rapidly, and then regressed. The transplanted tumors were anaplastic spindle cell sarcomas with numerous mitoses. The chromosomes of the tumors in the CH as well as those transplanted into the Syrian hamsters were CH chromosomes. Metastases appeared rather late in CH and were seen only in the lung, while the Syrian hamsters almost always showed metastases to the lymph nodes and lungs 6-8 wk. after inoc. Virus was demonstrated in both species by inj. of material from the tumors into chickens, where Rous sarcomas subsequently appeared. (See also CRA 1(5):#966, 1963.)

64-1541 AN ELECTRON MICROSCOPE STUDY OF RAUSCHER MURINE LEUKEMIA VIRUS. (Fr., Abstract) Levy, J.-P., M. Boiron, F. Hagueneau and J. Bernard. Sem. Hop. Paris 40(45-46-47-48):1946, 1964.

Electron microscope studies of the Rauscher murine leukemia virus showed that this virus measured 120 m (mµ?) in diameter and was provided with a head and a tail. The general aspect was that of a bacteriophage. Although the nature of the tail prolongation could not be determined, it differed from that of a bacteriophage.

See also abstract nos.: 1420, 1429, 1437, 1445, 1452, 1476, 1496

EPIDEMIOLOGY AND BIOMETRY

64-1542 THYROID DISEASES OBSERVED IN OKINAWA, JAPAN. (Jap.) Oshiro, T. (Oshiro Surg. Hosp., Naha, Okinawa, Japan), S. Kochi and T. Kadegawa. Geka (Surgery [Tokyo]) 25(5):503-507, 1963.

Among 334 cases of various thyroid diseases observed in Orientals in the authors' clinic in Okinawa during the period 1957-1961, 9 neoplasms were found: 1 Hürthle cell carcinoma (52-year-old female) and 8 papillary or follicular carcinomas (24-48 yr.).

64-1543 INCIDENCE OF ORAL MALIGNANT TUMORS. (E.) Ueno, T. (Dept. Oral Surg., Tokyo Med. Dent. U. Hosp., Japan), M. Shimizu, S. Shioda, A. Kotani, G. R. Hafiz and A. M. Raina. Bull. Tokyo Med. Dent. Univ. 8(1):71-81, 1961.

The 1,003 cases of all oral tumors admitted during the period 1930-1960 included 608 malignant tumors (carcinoma 540, sarcoma 68); 153 odontogenic tumors; and 242 benign tumors. The male:female ratio for all malignant cases was 1.60:1; for carcinoma alone, 1.66:1; that for sarcoma was only 1.19:1. Approx. 75% of these pts. were between the age of 40-69 yr. (range 2 mo.-88 yr.). The maxilla was the most common site (approx. 50%) of these malignant tumors; about 24% occurred in the mandible and 13% in the tongue. In 120 cases (44.1%) the carcinoma was associated with the accessory sinus. From the 608 pts., 540 biopsies were obtained which presented the following diagnoses: squamous cell carcinoma 65.8%; carcinoma simplex 8.3%; adenocarcinoma and others 7.1%; in addition there were various types of sarcoma.

64-1544 SOME PSYCHOLOGICAL AND CLINICAL BACKGROUND DATA ON THE ENVIRONMENTAL FACTORS WHICH AFFECT TUMOR FORMATION, CONSIDERED FROM THE STANDPOINT OF THE MEDICAL PRACTITIONER. (Ger.) Németh, G. (5 Gyori St., Budapest, Hungary) and M. Oó. Zschr. Psychosom. Med. 9(4):262-265, 1963.

In order to evaluate clinical and psychosocial factors conducive to the development of cancer, 100 pts. (28 males, 72 females) with various malignant diseases were interviewed. The malignancies included carcinomas of the breast (22), female genitalia (21), g.i. tract (17), lungs (6), bladder (4), prostate (3), thyroid (4); 6 were leukemias, 4 Hodgkin's disease, and 13 involved various sites. In 22 pts., a familial predisposition seemed likely. Manifestation of the tumor was preceded in 21 by infectious diseases, in 9 by mechanical trauma, in 31 by nonmalignant disorders involving the same organ. Also discussed is the role of psychological trauma, physical and emotional exhaustion due to stress and overwork and depressive tendencies; 49/100 pts. were rather optimistic. (See also CRA 2(8):#1422, 1964.)

64-1545 STUDIES ON THE PSYCHOSOMATIC ASPECT OF MALIGNANT TUMORS WITH THE AID OF RORSCHACH TESTS. (Ger.) Mezei, A. (77 Amerikai St., Budapest, Hungary) and G. Németh. Zschr. Psychosom. Med. 9(4):265-270, 1963.

As a continuation in depth of the work described in the preceding abstract, Rorschach tests were given to 50 cancer pts. (15 males, 35 females); 25 pts. with nonmalignant tumors were used as controls. The responses showed significant differences between the cancer pts. and the control group. Outstanding characteristics of the former were (1) extreme insecurity, manifested by severe self-criticism and doubt (34/50); (2) disintegration of the 'body concept', as evidenced by failure to come up with valid 'anatomy responses' (17/50); (3) loss of the functions normally used for interpretation, as shown by the pts.' tendency to ask the investigator for help (8/50); and (4) increased awareness of 'threatening' symbols (11/50). It is believed that cancer disease is associated with specific personality traits, which can be determined by means of Rorschach tests.

64-1546 BREAST CANCER IN THE NINTH AND TENTH DECADES. (E.) Leis, H. P., Jr. (Dept. Surg., New York Coll. Med., N. Y.), W. L. Mersheimer, J. Varadi and T. Hirose. J. Am. Geriat. Soc. 12(6):527-537, 1964.

After a review and discussion (33 references) of mammary cancer in the ninth and tenth age decades as well as the incidence according to parity, sex, race, occurrence in the right or left breast, the author reported that of 4188 women seen over the period of July 1952-1962, breast cancer developed in 2/96 (2.08%) pts. in the 90+ age group, and in 10/686 (1.45%) pts. in the 80-89 yr. age group, while among the total group, there were 51/4188 proved cases of breast cancer (1.21%) with the youngest of these pts. being 52-years-old. According to Dr. V. H. Handy, in 1960 in New York State, exclusive of New York City, 146 cases of breast cancer were reported in women 80-84 yr. of age and 108 cases in women 85 and older; the rates (per 100,000 population) reported for these 2 groups for 1958-60 were, resp., 311.95 and 365.53, representing increases over 2 previous periods, 1941-43 and 1949-51.

64-1547 CONSIDERATIONS ON THE MORBIDITY RATES OF SO CALLED SENILE ACTINIC KERATOSIS AND OF CUTANEOUS EPITHELIOMA IN A FISHERMEN'S COLLECTIVE. (Rum.) Balus, L. (Dept. Dermatovenerol., Ministry Health, Bucharest, Rumania) and V. Stoian. Dermatovenerologia (Bucur.) 9(3):225-230, 1964.

A study of 193 (191 men and 2 women) fishermen in a Rumanian Black Sea coastal village revealed 118

cases of senile keratosis (60%); 101 cases occurred in the age group past 40 yr. In addition, 2/193 had single, or multiple epitheliomas, 3/22 affected the lower lip. Most lesions were on the face. The 4 main reasons for these lesions are believed to be: 1. the dry continental climate of the Black Sea coast with 4-5 mo. of strong sunshine; 2. an av. exposure of about 10 mo./yr. to sun and weather; 3. the use and contact with liquid asphalt and tar used for the repair of boats; 4. the constitutional type of these fishermen: 15/193 had fair skin with little pigmentation, and red or light colored hair.

4-1548 TRENDS IN INFANT AND CHILDHOOD MORTALITY. 1961. (E.) Hunt, E. P. (Child Health Studies Br., Div. Res., U. S. Dept. Health, Education, Welfare, Washington, D. C.) and S. M. Goldstein. Statistical Series (76). U. S. Government Printing Office. Washington, D. C., 1964. 2 pp.

In the final table in this pamphlet, data are given which show a decrease in the death rate (per 100,000) from malignant neoplasms in children aged 1-14 yr. from 8.4 in 1951 to 8.1 in 1961. In the age group 1-4 yr., the decrease was from 10.8 in 1951 to 10.4 in 1961 whereas, in the age group 5-14 yr., there was an increase from 6.5 in 1951 to 7.1 in 1961.

-1549 ETIOLOGICAL AND CLINICAL ASPECTS OF PRIMARY CANCER OF THE LIVER. A STUDY OF 50 OBSERVATIONS. (Fr.) Girard, M., M. Plauchu, J.-P. Revillard. Lyon Med. 211(21):1415-1423, 1964.

see CRA 2(5):#957, 1964.

-1550 EPIDEMIOLOGY OF CANCER. (E.) Breslow, L. (Div. Prev. Med., California State Dept. Public Health, Berkeley). S. Afr. Cancer Bull. 8(2):63-69, 1964.

In a general discussion of the epidemiology of cancer, the author concludes that epidemiological studies as applied to cancer serve numerous purposes, including knowledge of the extent of cancer trends in time and distribution among the different segments of the population. Epidemiologic research in the past has helped in the control of disease, often long before specific etiologic agents were defined and can help in prevention and in treatment.

-1551 THE PATHOLOGY OF CARCINOMA OF THE NASOPHARYNX. (E.) Marsden, A. T. H. (Afr. Inst. Med. Res., Johannesburg). Med. J. S. Afr. (Johannesb.) 10(9):183-187, 1964.

Carcinoma of the nasopharynx is an uncommon form of cancer in most races (<1%), but high

frequencies (up to 10%) have been seen among Chinese, Malays, Dayaks and Filipinos. In a survey of 307 Chinese pts. with carcinoma of the nasopharynx, the av. age at diagnosis was 46.3 yr. and 106 of them were more than 40 yr. old. Incidence was negligible under 20 yr. and doubled with each decade until a max. was reached in the sixth decade. There were 216 males and 91 females (2.4:1), but this male preponderance was seen chiefly from the sixth decade on. The etiology remains unknown, although many carcinogens have been implicated; an additional factor may be needed to explain the high male sex ratio after age 50 in Chinese men.

64-1552 CASE CLUSTERS IN THE OCCURRENCE OF LEUKAEMIA AND CONGENITAL MALFORMATIONS. (E.) Heath, C. W., Jr. (Hemat. Lab., Boston City Hosp., Mass.), M. D. Manning and L. Zerkowicz. Lancet 2:136-137, 1964.

An unusual prevalence of births associated with congenital heart disease was observed in Niles, Illinois, at the same time as an increased prevalence of childhood leukemia (see CRA 1(5):#978, 1963). In Orange, Texas, 3 cases of leukemia in children occurred within a period of 9 mo. in families that lived within one-half mile of one another. In families in widely separated areas of the town there was a cluster of births of 5 infants with congenital heart disorders within a short period about 1 yr. later. The father of one of the latter children developed leukemia during the same period. These findings raise the possibility of an epidemiological relation between some types of leukemia and some congenital malformations.

64-1553 SOCIAL FACTORS FOR THE ADULT DISEASES AMONG THE MALES IN JAPAN. (E.) Sato, T. (Dept. Nutr. Biochem., Inst. Public Health, Tokyo). Bull. Inst. Publ. Health 13(1):56-58, 1964.

In an effort to correlate socioeconomic status with the incidence of some 21 disorders, the author tabulated the number of male deaths from specific causes reported in newspaper obituaries over a 2-year period (A) vs. the (estimated) total number of male deaths from the same specific causes within corresponding age groups in Japan as a whole during the same period (B). The resulting ratio (A/B = C) was considered an index of the relative percentage frequency of each disorder among the "upper class". The ratios derived for reported neoplasms were as follows: stomach, 0.83; rectum, 3.0; lung, 2.9; liver, 1.7; esophagus, 1.6; maxillary sinus, 5.0; prostate, 2.5; reticulum cell sarcoma, 6.5; acute leukemia, 7.7. Thus deaths due to stomach cancer were lower in the obituary group compared to all of Japan, but the rate was still much higher than that of the USA (Japan:USA, 597/150). The differences noted relative to leukemia may be related to the type of facilities available for diagnosis. Liver,

prostate and rectum cancer appeared to be higher among the obituary group, which, in general, consisted of wealthier people living in better heated houses and who were better nourished.

- 64-1554 MALIGNANT LYMPHOMA OF THE TESTIS. (E.)
Gowing, N. F. C. Brit. J. Urol.
36(2) (Suppl.):85-94, 1964.

Among 63 pts. with malignant lymphoma of the testis, only 1 was a child, aged 2; 51 cases (80%) occurred in pts. over 50. The initial swelling was right-sided in 32/63 and left-sided in 29/63, indicating that subsequent bilateral involvement tended to be successive rather than synchronous. Only 6/63 showed evidence of lymphoma prior to swelling of the testis (3/6, intranasal), although 8/63 showed clinical evidence of disseminated lymphoma at the time of orchiectomy. A history of trauma was given in 3 cases: 1, many yr. before; 1, 20 mo. before; 1, shortly before the appearance of testicular tumor. In no case was the tumor associated with cryptorchidism. Three cases of testicular involvement secondary to plasma cell tumors at other sites are also reported.

- 64-1555 PROBLEMS IN FOLLOW-UP CARE IN CANCER THERAPY. (Ger.) Gebhardt, K.-H.
(1st. Clin. Med., City Hosp., Karlsruhe, Germany).
Med. Klin. 59(37):1468-1471, 1964.

Cancer mortality in USA, France, Germany, Italy, and England is tabulated and shows an absolute and a relative increase within the last 3 decades. The relative mortality (per 100,000 population) in 1960 was highest in England (430), followed by France (388.7), Germany (388.4), USA (295.9), and Italy (280.3). This rise in cancer mortality is attributable in part to improved diagnostic techniques, and in part to the prolonged life span and to increased environmental noxae.

- 64-1556 BIOMETRIC ASPECTS OF CANCER OF THE BREAST IN BIOPTIC MATERIAL OF THE HISTOPATHOLOGIC DIVISION OF THE CENTER FOR THE DIAGNOSIS AND CURE OF TUMORS (CPDCT) OF THE PROVINCE OF PERUGIA. (It.) Bucciarelli, E.
(Inst. Anat., U. Perugia, Italy). Lav. Ist. Anat. Univ. Perugia 24(1):57-63, 1964.

An analysis of the data accumulated over a period of 22 yr. (1942-1963) at the CPDCT of Perugia, Italy, showed that among a total of 7,243 malignant primary tumors, the percentage of distribution by site was: breast, 16.07; uterus body and cervix, 14.23; stomach and duodenum, 11.84; intestine, 8.65; skin, 7.57; nasopharynx and respiratory system, 7.4; lymph glands, 5.92; lip, tongue and oral cavity, 4.48; kidney and bladder, 3.78; bone and striated muscle, 3.27; other, 16.74. In females with cancer of the breast, the av. age at the time of diagnosis was 52.83 yr.;

the majority of mammary cancers occurred between 46 and 65 yr. of age. The distribution curve arranged in 5-year cohorts was bimodal; the two periods of highest frequency corresponded to the periods preceding and following menopause. In males with cancer of the breast, the av. age at the time of the diagnosis was 65.5 yr.

- 64-1557 CANCER AND ATMOSPHERIC POLLUTION. (E.)
Pybus, F. C. (Dept. Surg., U. Newcastle/Tyne, England). Med. Proc. (Johannesb.) 10(12): 242-254, 1964.

In this historic review and discussion, the following aspects of cancer and atmospheric pollution are considered: experimental production of cancer in animals with tar; tar and soot as a cause of cancer in humans; benzyrene (BP) in tar, soot and smoke; the nature and sources of smoke in the atmosphere and its BP content; and confirmatory evidence for smoke as a cause of cancer. When the major sources of atmospheric pollution in Great Britain are considered in terms of their BP content the results were: coal, 300 parts/million parts of free carbon (total 750 tons); motor fuel (inefficiently operating engines), 14-120 $\mu\text{g}/\text{m}^3/\text{min.}$; garden and other rubbish, 70 $\mu\text{g}/\text{million}$ of free carbon; tobacco, 0.2 $\mu\text{g}/\text{million}$ of free carbon. The fact that the BP content per yr. from cigarette smoke is only 1/200,000 that contributed by coal smoke in Britain may well explain why in 2 separate studies (from New Zealand and South Africa) British immigrants showed a much higher death rate from lung cancer than the native populace, even when the latter were by far the heavier smokers. A correlation has been demonstrated between area smoke conc. and the incidence of lung, stomach and intestinal cancer. (See also the following abstract.)

- 64-1558 CANCER AND ATMOSPHERIC POLLUTION. (E.)
Pybus, F. C. (Dept. Surg., U. Newcastle Tyne, England). Med. Proc. (Johannesb.) 10(13): 268-277, 1964.

In a continuation of the review (37 references) and discussion presented in the preceding abstract, the following topics are discussed: tobacco smoking and cancer (the author feels the emphasis here is proportionally too great); other causes of cancer (radiation, body secretions, food and dyes); the nature of cancer (embryology and growth of cells, treatment); susceptibility (differences of species, race, etc.); cancer in animals (effect of environment); diagnosis and treatment; the antiquity of smoke and cancer; cancer education (medical, local government controls and the press); legislation against pollution; the cost of atmospheric pollution. The author concludes that smoke from industrial and domestic sources constitutes the main source of aerial pollution and that legislative controls of these sources should be enacted because cancer is an eminently preventable disease.

64-1559 SMOKING AND HEALTH. (E.) Lovegrove, T. (Wongan Hills, Western Australia). Med. Aust. 2(5):197, 1964.

In a brief discussion of lung cancer, it is felt that more attention should be directed toward other etiologic agents than cigarette smoking. It is pointed out that heavy cigarette smokers in the Transvaal seem to be unaffected and that lung carcinoma is commoner in Western Europe and the USA than in the USSR and satellite countries where a different method of curing cigarette tobacco prevails. The author and 2 colleagues in the Western Australian wheat belt have seen only one primary lung cancer in 10 or more yr. in an area of 6,000 square miles with a population of about 6,000.

64-1560 CHORION-CARCINOMA IN THE MIDLANDS. (E.) Mills, W. (United Birmingham Hosp., England). Clin. Radiol. 15(3):260-262, 1964.

The incidence of choriocarcinoma in the author's material was estimated as 1/43,000 deliveries in contrast to 1/1331 deliveries reported from Hong Kong) during a 15-year period. Among the cases reported age incidence was 12 between 15-30, 7 between 31-40, 4 over 40. The author suggests an etiologic relationship to fertility rather than chronological age. In 9/23 (39%), the cancer was associated with or followed hydatidiform mole (other published percentages, 44 and 50). One pt. had had 3 children and 3 hydatidiform moles (the last, 2 yr. prior to the diagnosis of choriocarcinoma). In one pt. choriocarcinoma was diagnosed 6 yr. following hysterectomy for a supposedly benign mole; in 1/23, 1 mo. after a successful pregnancy; in 4/23, shortly after abortion; in 1/23, in association with an ectopic tubal pregnancy. In 8/23, no relationship to a preceding pregnancy could be demonstrated.

64-1561 STATISTICS. (Hun.) Editorial. Magy. Onkol. 8(2):69-71, 1964.

In a report from the State Institute of Oncology, Nagy states that for all of Rumania for the years 1959 and 1960, the incidence (per 100,000 men) of mammary cancer was 28.6 and 30.2, resp. incidence (percentage) before age 40 was 7.9; 40-49, 20.8; 50-59, 28.5; 60-69, 25.9; over 70, 16.4. L. Tapolcsányi states that during the period 1955-1962 mammary cancer constituted 10.7-17% of all cancer treated by the Institute.

64-1562 THE RELATIONSHIP BETWEEN GASTRIC ULCER AND GASTRIC CANCER. (E.) Aagaard, P. (Dept. Surg., Rigshospitalet, Copenhagen, Denmark). Acta Chir. Scand. (Suppl. 318):70-79, 1964.

The author reports a 10% diagnostic error with regard to the cases heretofore reported of malignant transformation of gastric ulcer. Sex distribution was found to be of no importance, while age distribution merely showed gastric ulcer to appear in older pts. and duodenal ulcer to appear in younger pts. The incidence of combined gastric and duodenal ulcer and the rarity of coexisting duodenal ulcer and gastric cancer are also discussed. It is pointed out that many studies of combined duodenal ulcer and gastric cancer unjustifiably include cases where resection for ulcer had been performed before carcinoma developed.

64-1563 MORTALITY IN RELATION TO SMOKING: TEN YEARS' OBSERVATION OF BRITISH DOCTORS. (E.) Doll, R. (Coll. Hosp. Sch. Med., U. London) and A. B. Hill. Brit. Med. J. 1:1399-1410, 1964.

Survivors of a survey of smoking habits of British doctors conducted in 1951 were sent second questionnaires in 1958, and calculated standardized mortality rates in relation to smoking for all ages were obtained. Total deaths include 4,597 men and 366 women. Among male doctors, a steadily rising death rate (per 1,000) was seen for lung cancer mortality with increasing consumption of cigarettes at every age above 45 yr. For each type of smoking (cigarettes alone, mixed, pipe and/or cigars alone) the lung cancer death rate in continuous smokers was higher than that of those who had stopped, while the rate in ex-cigarette smokers (0.24) was notably less than that in current pipe smokers (0.47). Lung cancer death rate for those who had given up smoking was 19% lower than the rate for continuing smokers. According to histologic type mortality ratios (with standard death rate of continuing cigarette smokers = 100%) for those smoking 1-14, 15-24 and 25 or more cigarettes/day, resp., in those in the squamous group was 68%, 104%, and 139%; in the oat cell and anaplastic group 44%, 91% and 169%. Of deaths from other cancers considered (oropharynx, nose, larynx, esophagus), only cancer of the esophagus shows a progressive increase in mortality with increased smoking and a marked reduction in those who have stopped. In men who have given up smoking, mortality rates from lung cancer were found to decline immediately and became progressively smaller as the length of time increased since smoking had been given up. While mortality from all causes was slightly higher in inhalers (17.73) than in non-inhalers (15.83), the largest relative excess was observed with lung cancer (71%). Among women doctors, total mortality among cigarette smokers was identical with that among non-smokers. Lung cancer mortality was highest among women who smoked 15 or more cigarettes a day. The age at which smoking started and different inhaling habits were found to be influencing factors. (See also the following abstract.)

64-1564 MORTALITY IN RELATION TO SMOKING: TEN YEARS' OBSERVATIONS OF BRITISH DOCTORS.

(E.) Doll, R. (Coll. Hosp. Sch. Med., U. London) and A. B. Hill. *Brit. Med. J.* 1:1460-1467, 1964.

The authors present an interpretation of the various observations made in the preceding abstract. The linear rise seen in annual death rates from cancer of the lung from nonsmokers to light smokers to medium smokers to heavy smokers indicates no smoking threshold which must be reached before the death rate from cancer of the lung shows a response. The mortality drop in subjects giving up smoking can be explained in terms of a diminishing risk from the previously operative environmental agent, but not in terms of genetic selection of those who choose to give it up. The decline in lung cancer mortality among doctors, as compared to the increase (22%) in all men more than 25 yr. old, for the period 1952-61 is attributed to a change in the smoking habits (giving up and reduced consumption) of the former. The very low death rate from lung cancer in urban areas does not suggest that air pollution *per se* has been an important factor, while a synergistic action has not been definitely proven. (See also the preceding abstract.)

64-1565 CANCER RESEARCH. (E.) Case, R. A. M. (Chester Beatty Res. Inst., London, S.W.3). *Lancet* 2:309-310, 1964.

The author believes that a further detailed and independent investigation of the hazard in the rubber industry is needed (despite a recent statement from a rubber manufacturer's association) because the epidemiological problems posed by such a complex situation require a considerable background knowledge of the population that has been exposed to risk and an analysis of the dynamics of the epidemic of bladder cancer that has affected the rubber industry. Further recent investigation of mortality of some rubber workers due to bladder tumors indicates a further continued and even more rapid rise.

64-1566 MORTALITY BY INDUSTRY AND CAUSE OF DEATH (AMONG MEN 20 TO 64 YEARS OF AGE). (E.) Guralnick, L. (Ed.) (Mortality Statistic. Br., U. S. Dept. Health, Educ., Welfare, Washington, D. C.). *Vital Statistics (Spec. Rep.)* 53(4):341-347, 1963.

Statistical report on causes of death, in 1950, of men aged 20-64 yr., with work experience, classified by site of neoplasm and by industry. (See also CRA 2(7):#1375, 1964.)

64-1567 MORTALITY BY OCCUPATION LEVEL AND CAUSE OF DEATH (AMONG MEN 20 TO 64 YEARS OF AGE). (E.) Guralnick, L. (Ed.) (Mortality Statist. Br., U. S. Dept. Health, Educ., Welfare, Washington, D. C.). *Vital Statistics (Spec. Rep.)* 53(5):439-612, 1963.

Statistical report on the causes of death, in 1950, of men aged 20-64 yr., with work experience, classified by site of neoplasm and by industry. This report supplements an earlier one (Vol. 53, No. 4) covering other occupations.

64-1568 HEALTH CONDITIONS IN THE AMERICAS 1961-1962. (E.) Horwitz, A. (Director). Sci. Publ. No. 104, Aug. 1964. Pan Am. Health Organ. World Health Organ., Washington, D. C., pp. 1-70.

A large section of this report by the Pan American Health Organization deals with deaths, including those from neoplasms (both numbers and rate/100,000), in 22 countries with a detailed analysis for 1961 or 1962. In a separate listing of the 5 principle causes of death for each country, neoplasms rank 1-5 for 15/22; the exceptions were Colombia, Ecuador, El Salvador, Guatemala, Honduras, Mexico and Nicaragua. In a listing of the 5 principle causes of death for age groups under 5, neoplasms are included only for the U. S., Canada and Uruguay. The following 4 causes of death ranked variously 1 to 5: 1. Certain diseases of early infancy (21 countries); 2. Gastritis, enteritis, etc. (16 countries); 3. Diseases of the heart (17 countries); 4. Malignant neoplasms (15 countries).

64-1569 CANCER MORTALITY IN FRANCE IN 1962. (Fr.) Flamant, R. (Dept. Cancer, Nat. Inst. Hyg. Villejuif, Seine), L. Maujol and O. Lasserre. *Bull. Inst. Nat. Hyg.* 19(1):21-52, 1964.

Based on statistics obtained from the National Institute of Statistics and Economic Studies, reported cancer deaths (per 100,000 population; including leukemias) in France for the yr. 1962 were 223 (males), 184 (females) and 203 (both sexes). Probable total cancer deaths were estimated at 227 (males), 163 (females) and 191 (both sexes). A slight progressive decrease was seen in cancer mortality from age 0-9 yr. and a steady increase from 10 yr. old on, reaching a peak at 85 yr. old and over was seen in males, females and both sexes combined. Expressed as percentage, the most frequent cancer sites were, in males, stomach 14.1%, bronchopulmonary 13.9%, prostate 9.2%, and esophagus 7.9%; in females, breast 14.1%, stomach 13.2%, intestine excluding rectum 11.8%, and uterus 7.7%; in both sexes combined, stomach 13.6%, intestine excluding rectum 9.2%, bronchopulmonary 9.0%, and breast 6.7%. Comparison of these mortality rates with those for 1952 has shown a marked increase in bronchopulmonary cancer (from 17.9 to 31.9) in males and in leukemia in both sexes. Highest cancer mortality rates were seen for the Departments of Seine, Seine-et-Oise, Manche, Calvados, Seine-Maritime and Haut-Rhin; very low cancer mortality rates were seen for Aveyron (all cancers) and Lozere and Ardèche

leukemias). For a previous paper on cancer mortality in France from this Institute see CRA 2(1): 112, 1964.

4-1570 COMPARABILITY RATIOS. (BASED ON MORTALITY STATISTICS FOR THE FIFTH AND SIXTH REVISIONS.) (E.) Faust, M. M. (U. S. Dept. Health Educ. Welfare, Washington, D. C.) and A. B. Dolman (Eds.). Vital Statistics (Spec. Rep.) 51(2):133-178, 1963.

First report of a comparison of the mortality statistics of the U. S. for 1950 classified according to the Fifth and Sixth Revisions of the International List of Diseases and Causes of Death. Figures are included on malignant neoplasms, classified in detail by site.

4-1571 COMPARABILITY RATIOS. (BASED ON MORTALITY STATISTICS FOR THE FIFTH AND SIXTH REVISIONS.) (E.) Faust, M. M. (Mortality Statist. Br., U. S. Dept. Health, Educ., Welfare, Washington, D. C.) and A. B. Dolman (Eds.). Vital Statistics (Spec. Rep.) 51(3):181-245, 1964.

Second report of a comparison of the mortality statistics of the U. S. for 1950, including information of malignant neoplasms, classified by site as well as by sex and race of host.

4-1572 AN EPIDEMIOLOGIC APPROACH TO THE LYMPHOMAS OF AFRICAN CHILDREN AND BURKITT'S CARCINOMA OF THE JAWS. (E.) Daildorf, G. (Loan-Kettering Inst., New York), C. A. Linsell, E. Barnhart and R. Martyn. Perspect. Biol. Med. 7(4):435-449, 1964.

A survey conducted during 1957-61 and based on information from the Kenya Cancer Registry and on field and laboratory investigation, malignant lymphomas and Hodgkin's disease were found to constitute 12% and 25%, resp., of the 2,737 tumors encountered in Kenya. Corresponding figures were seen in an analogous survey conducted in Tanganyika. In both Uganda and Kenya, lymphomas accounted for 50% of childhood malignancies. The incidence of lymphomas and squamous carcinomas is approx. the same in all Kenya tribes and geographic regions, while the childhood lymphomas showed marked variation in rates. For 100,000 inhabitants, childhood lymphoma incidence among the Bantu was 8.2 in coastal areas, 2.0 in the

central highlands and 1.2 in the highland belt. A review (37 references) of the possible etiologic significance of social conditions, diet, local background radioactivity, tumorigenic viruses and malaria is also included. (See also CRA 2(3): #533; and ibid., (8):#1525, 1964.)

64-1573 CLINICAL STUDY OF PRIMARY PULMONARY CARCINOMA COMBINED WITH PULMONARY TUBERCULOSIS. (Jap.) Ito, K. (Nagoya U. Sch. Med., Japan), Y. Saito, Y. Nishimura and M. Ando. Kekkaku (Abstr. Current Lit. Tubercul.) 38(3): 119-121, 1963.

Among 141,045 and 150,045 Orientals studied in a mass examination in 1961 and 1962, resp., 6 cases of primary pulmonary carcinoma (PPC) were found each year. Among a total of 3,346 pts. with pulmonary tuberculosis (ptb) over age 40 who were followed up more than 3 yr., 5 pts. had PPC giving a rate (per 100,000) of 48.8 (68.7 in males, 36.5 in females). Among 232 pts. with PPC there were 35 cases (15.1%) of ptb. While prevalence of ptb in the group over age 40 was 9.7%, incidence of cancer combined with ptb was higher in 4th, 5th and 6th decades (in decreasing order). Cancer and ptb lesions were observed simultaneously in the same segment of the lung in only 3 pts.

64-1574 AIR POLLUTION WITH CANCERIGENIC SUBSTANCES. (E.) Kotin, P. Acta Un. Int. Cancr. 19:469-471, 1963.

64-1575 USEFUL ETIOLOGIC AND PATHOGENIC CONCEPTS IN THE DIAGNOSIS, PREVENTION AND TREATMENT OF CANCER OF THE ESOPHAGUS. (Sp.) Ramos, P. (Dept. Health, University City, Mexico, D. F.). Rev. Gastroent. Mex. 27(159):239-244, 1962.

According to the latest available statistics from Mexico the number of deaths due to cancer of the esophagus was 143 (115 in the States and 28 in D.F.) in 1952; 163 (136 in the States and 27 in D.F.) in 1956; 201 (155 in the States and 46 in D.F.) in 1958; and 207 (166 in the States and 41 in D.F.) in 1959. In 1958 and 1959 the male:female ratio was 105:50 and 102:64, resp., for the States; 35:11 and 27:14, resp., for D.F. In recent epidemiologic studies, alcohol and tobacco have been found to play a role in the pathogenesis of this condition.

See also abstract nos.: 1423, 1427, 1435, 1458, 1504

MISCELLANEOUS

- 64-1576 HISTOGENESIS OF ENDOMETRIAL CARCINOMA. (E.) Gray, L. A. (Dept. Path., U. Louisville Sch. Med., Kentucky) and M. L. Barnes. Ann. Surg. 159(6):976-986, 1964.

Histological sections from 109 pts. with adenocarcinoma of the endometrium, where both tumorous and uninvolved tissue were available, were divided into 5 groups: Group I, premenopausal; Group II, postmenopausal with prolonged estrogen therapy; Group III, postmenopausal, (intrinsic estrogen); Group IV, postmenopausal (atrophic smear); Group V, no smears. Among these groups (total cases in parentheses) the incidence of hyperplasia, atypical hyperplasia and polyps were: Group I (28), 14, 16 and 8; Group II (13), 9, 9 and 7; Group III (4), 4, 2, and 3; Group IV (13), 7, 4 and 4; and Group V (51), 22, 19 and 24, resp. Total incidence of these conditions was 66%. From these data, the authors cite endometrial hyperplasia after menopause and atypical hyperplasia to be the most incriminating as precancerous lesions. The evidence suggests that other agents besides estrogens may be causes for premalignant changes in the endometrium.

- 64-1577 ENDOPLASMIC RETICULUM AND HEPATIC CARCINOGENESIS. (E.) Pitot, H. C. (McArdle Mem. Lab., U. Wisconsin Sch. Med., Madison) and C. Peraino. Pp. 139-149 in Biochemical Clinics. Vol. 3: The Liver. Kugelmass, I. N. (Ed.). Reuben H. Donnelley Corp. (Publ.), New York, 291 pp., 1964.

As a possible explanation for hepatocarcinogenesis, the authors discuss the effect of carcinogens upon the endoplasmic reticulum (ER), the major site of protein (enzyme) synthesis in the normal liver cell, and upon the metabolic processes connected with this organelle. The carcinogen acts on the ER and alters its structure irreversibly; this structural alteration results in a change in the rate of production of various enzymes and a loss in the ability of the synthesizing machinery of the cell to respond normally to exogenous regulators (amino acids, hormones, glucose). If the alterations still permit cell viability and protein synthesis, the altered cell will then grow relatively autonomously. Various corollaries to this hypothesis of structural-functional membrane defects are presented. (See also CRA 2(4):#657, 1964.)

- 64-1578 SEMINOMA OF THE UNDESCENDED TESTICLE. (It.) Covarelli, E. (Inst. Gen. Clin. Surg., U. Perugia, Italy). Ann. Fac. Med. Perugia 55(2):287-293, 1963.

Two cases are presented of seminoma of the undescended testicle: a 29-year-old man with a seminoma of the abdominal testis and a 38-year-old man with the rare association of seminoma of

the inguinal testis and homolateral renal agenesis. In both cases, the tumor developed in partially mature and functioning testes. A review (24 references) of the incidence, symptomatology and surgical management of tumors developing in the ectopic testicle is presented.

- 64-1579 SQUAMOUS CELL CARCINOMA OF THE RECTUM COMPLICATING ULCERATIVE COLITIS: REPORT OF TWO CASES. (E.) Hohm, W. H. (Mayo Found., Rochester, Minn.) and R. J. Jackman. Proc. Mayo Clin. 39(4):249-251, 1964.

The cases of two women are presented in which squamous cell carcinoma of the rectum appeared as a complication of ulcerative colitis (UC). In 1 pt. the carcinoma occurred at the age of 34 yr., 9 yr. after the diagnosis of UC; in the second pt. at 51 yr. of age, 25 yr. after diagnosis. The development of squamous cell carcinoma, rather than adenocarcinoma, in the region proximal to the mucocutaneous junction is rare.

- 64-1580 THE CUNA MOON-CHILD SYNDROME. (E.) Keeler, C. (Dept. Med. Genet., Milledgeville State Hosp., Ga.). Derm. Trop. 3(1):1-11, 1964.

Comparative clinical, anthropometric and psychiatric studies were conducted in Panama upon brown-skinned Cuna Indian and albino Cuna Indian Moon-Children. All of the 35 albino Indians observed showed skin abnormalities, as a result of prolonged exposure to the sun, ranging from freckles and keratoses to skin cancer. The severity of the skin condition increased in both sexes with age. Although the av. age was less in males than in females, skin lesions were more severe in the former because of greater overall exposure. Biopsy of 10 carcinomas revealed that 8 were squamous cell, 2 were basal cell; previous studies showed only squamous cell carcinomas among Moon-Children. Of 6 of these Indians (age 21-36) with the Cuna Moon-Child syndrome observed at the Milledgeville State Hospital, 1 showed a squamous cell carcinoma on the left cheek, 2 showed squamous cell carcinomas on the right cheek and 1 showed a squamous cell carcinoma on the right shoulder and basal cell lesion on the left temple. The authors conclude that the alterations observed in morphology and behavior are pleiotropic manifestations of the albino gene, similar to alterations found associated with the presence of certain coat color genes in mammals.

- 64-1581 FURTHER OBSERVATION ON THE ROLE OF ANEUPLOIDY IN ACUTE LEUKEMIA. (E.) Reisman, L. E. (Child. Hosp. Michigan, Detroit), W. W. Zuelzer and R. I. Thompson. Cancer Res. 24(8):1448-1455, 1964.

In an updating of CRA 2(2):#384, 1964, 6 additional

children (age 2-7 yr.; 5/6 with lymphoblastic stem cell leukemia) were added to the 7 cases previously reported in which specimens were obtained for chromosome studies before the initiation of therapy. All showed initial aneuploid karyotypes with modal distributions ranging from 47 to 65. Immediately after diagnosis pts. were treated with various chemotherapeutic agents which included: steroids, 6-mercaptopurine, methotrexate (MTX), cyclophosphamide and vincristine. During remission the normal diploid mode was restored, regardless of the duration of the disease or the therapy employed. In the second (or third) relapses studied, the originally observed aneuploid karyotype always re-emerged after remissions of various lengths up to 4 mo. The observations described conclusively support the thesis that the aneuploid cells dominant in the active stage of leukemia represent true stem lines. (See also RA 1(9-10):#1825, 1964.)

4-1582 CHROMOSOMAL CHANGES IN HUMAN LEUKEMIA. ACUTE LEUKEMIA. SECOND REPORT. (Rus.) Sessarskaia, T. P. (Cent. Inst. Haematol. Blood Transf. (Order Lenin), Moscow), G. V. Osechenskaia and S. A. Khrustalev. Probl. Gemat. 9(6):10-15, 1964.

Studies of chromosome structure, size and number are described in 3 male pts. with acute leukemia treated with cytostatics (6-mercaptopurine and azauracil riboside).

4-1583 PREDISPOSITION TO SPONTANEOUS TUMOR AND LEUCOPOIESIS IN MICE. (E.) Parfentjev, A. (Inst. Appl. Biol., New York, N. Y.), J. E. Marino and R. Jonnard. Oncologia (Basel) 17(3-4):27-235, 1964.

To examine the role of the spleen in neoplastic conditions, leucopoiesis in non-tumor bearing C3H/HeJ (tumor-susceptible) and C57BL/6J (tumor-resistant) strains of mice was compared with previously published work on CFW tumor-bearing mice. Splenectomy and/or vaccination with pertussis produced increased WBC in all 3 strains. Vaccination produced increased granulocytosis in intact and splenectomized tumor-bearing CFW mice, normal 2-3 mo. old C3H/HeJ mice and in previously splenectomized 1.2-1.7-month-old C3H/HeJ mice; splenectomy alone was not followed by increased granulocytosis. The data indicate that pertussis vaccine might be blocking functions of the spleen and that the spleen may regulate the level of granulocytes in the circulating blood and be involved in resistance to neoplastic growth.

4-1584 SILICO-TUBERCULOSIS AND LUNG CANCER. (It.) Pietrojusti, M. (Ministry Health, Rome). Radiol. Prat. 13(4):367-378, 1964.

After an extensive review of the literature (23 references) regarding the etiological significance

of silicosis in lung cancer, the author concludes that silico-tuberculosis (unlike asbestosis or siderosis) cannot be considered a determining factor in lung cancer. This is based on the following conclusions: silicosis may act as a co-factor when predisposition is present either in the tissue or organ involved; silicotic pts. die at a relatively younger age than lung cancer pts.; low percentage (6.9%) of lung cancer in silicotic pts. with respect to total cancer cases studied. It is suggested that silicon may act indirectly as a carcinogen by inducing diffuse or localized alterations in pulmonary or bronchial tissue which may predispose to the development of cancer.

64-1585 EXISTENCE OF TWO VARIETIES, 17 S OR 18.3 S, OF γ 1M SERUM GLOBULINS, AND OF AN INCREASE IN 6.6 S SERUM GLOBULINS IN WALDENSTROM'S DISEASE. (Fr.) Filitti-Wurmser, S. (Physicochem. Biol. Inst., U. Paris, Sorbonne), C. Gentou and L. Hartmann. Rev. Franc. Etud. Clin. Biol. 9(4):398-410, 1964.

The sera of 57 untreated pts. with Waldenström's disease (WD) were analyzed by means of ultracentrifugation, microelectrophoresis, and various routine tests for serum proteins. The mean conc. of heavy constituents (peak "M") was 32.5 g/l (range 8-70 g/l). The sedimentation constants of the principal heavy constituent, M₁, varied between S_{20W} = 15.6 and S_{20W} = 19.3; this difference exceeds the technical error and suggests actual differences between the macroglobulinemic components. Distribution of the cases as a function of the constant of M₁ showed 2 modes coinciding with the arithmetic means at 17 S and at 18.3 S, resp. The conc. of the components M₂ and M₃ varied with that of M₁. A statistically significant increase in peak "G" was demonstrated. A decrease in peak "A" was generally associated with a decrease in plasma albumin. The possibility is discussed that the γ 2-globulins produced by lymphatic or lymphoreticular cells may in turn give rise to macroglobulin complexes (γ 1M-globulins). The cytological differences between WD and multiple myeloma have thus become very indistinct; both diseases are based on a disturbance in γ 2-globulin synthesis, and the production of one or the other type of abnormal globulin might depend on the degree of cellular dystrophy.

64-1586 INFLAMMATORY STIMULATION OF THE RES WITH SUBSEQUENT RETICULOSES. (Ger.) Scheuer-Karpin, R. (1st Med. Clin., Hufeland Hosp., Berlin/Buch). Folia Haemat. (Leipzig) 81(3):257-264, 1964.

After analysis of the histories of 95 pts. with chronic lymphatic leukemia and other irreversible diseases of the RES (excluding myelocytic and stem cell type leukemia), 63 showed a wide variety of chronic or recurrent inflammations. It is suggested that such stimulation of the RES may play a role in the etiology of these diseases. Two

cases are presented which show the transition from reactive to irreversible reticulosis with or without leukemia. A review of literature is also presented (17 references).

64-1587 CHROMOSOMES OF LYMPHOSARCOMA AND CANCER CELLS IN BONE MARROW. (E.) Sandberg, A. A. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. Ishihara, Y. Kikuchi and L. H. Crosswhite. Cancer 17(6):738-746, 1964.

The karyotypes of bone marrow cells were examined in 6 pts. with lymphosarcoma (LS; 2 boys aged 6 and 14 yr.; 4 men aged 22-61 yr.) and in 2 pts. (a 67-year-old man with primary cancer of the lung at autopsy; a 66-year-old man with suspected cancer of the prostate) with cancer cells in the bone marrow (CBM). Treatment of LS pts. included X-rays, nitrogen mustard, vinblastine, cyclophosphamide, vincristine, chlorambucil, AB-132 or 6-mercaptopurine; CBM pts. were untreated. In LS pts., abnormal cells were characterized by hyperdiploidy and a variety of chromosome modes ranging from 46 to 82; marker chromosomes were present in some of the metaphases. The karyotypes of pts. with CBM were highly abnormal and were dissimilar from each other and from those of LS cells. None of the cells resembled one another in karyotype, but all cells seemed to be cytogenetically allied to cancer cells. The frequency of hyperdiploid karyotypes appears to be related to the number of abnormal cells in the marrow, disappearing with remission and reappearing with relapse. (See also CRA 1(5):#1011, 1963; and *ibid.*, 2(2):#382, 1964).

64-1588 HYPERTROPHIC GASTRITIS WITH MALIGNANT DETERIORATION AND METASTASIS TO BONE. (E.) Pear, E. G. (Dept. Int. Med., St. Joseph Mercy Hosp., Pontiac, Mich.) and R. Horsch. Am. J. Gastroent. 42(3):280-284, 1964.

A case is reported of a 54-year-old man with hypertrophic gastritis (giant fold interstitial type) diagnosed 7 yr. prior to his death and treated medically at repeated hospitalizations. During this period it is believed that the gastric mucosa underwent malignant deterioration with metastases to much of the body including bone.

64-1589 DISEASES OF HYPERSENSITIVITY AND CHILDHOOD LEUKEMIA. (E.) Fraumeni, J. F., Jr. (NCI, Bethesda), M. D. Manning and C. R. Stark. J.A.M.A. 188(5):459, 1964.

A survey was conducted among 498 children under age 16 with leukemia (diagnosed between 1958-61) and their relatives to evaluate the role of allergy and rheumatic disease. No conclusive case-control differences were found for either allergic (including atopic allergies such as asthma, hay fever and eczema), rheumatic or arthritic disease in these children or in their close relatives. It is concluded that children

with leukemia have neither a personal nor a familial diathesis for allergic or rheumatic (collagen) disorders.

64-1590 CYSTIC FIBROSIS AND NEOPLASMS OF THE MAMMARY GLAND AT A YOUNG AGE. (It.) Trentini, G. P. (Inst. Path. Anat., U. Modena, Italy) and C. Barbanti Silva. Arch. De Vecchi Anat. Pat. 40(2):627-651, 1964.

Described are 6 cases of fibrocystic mastopathy occurring in 10-16-year-old girls, one case of intracystic benign papilloma in a 17-year-old girl, and one case of intraductal mammary carcinoma in a 19-year-old woman. The latter was the only case found in a woman below 20 yr. of age among a total of 1200 breast carcinomas in females which came under observation at the Institute during a 15-year period prior to this report. The authors describe in addition a case of intra- and extra-ductal mammary carcinoma which developed in a 30-year-old woman approx. 4 mo. after delivery. The etiology and pathogenesis of these conditions in relation to disturbances of the endocrine system (mostly the ovary at a young age) are discussed and much pertinent literature reviewed (90 references).

64-1591 THE DEVELOPMENT OF MALIGNANT LYMPHOMA IN THE COURSE OF SJÖGREN'S SYNDROME. (E.) Talaí, N. (NIH, Bethesda) and J. J. Bunim. Am. J. Med. 36(4):529-540, 1964.

See CRA 1(11):#2031, 1964.

64-1592 THE RELATION BETWEEN THE RETICULOENDOTHELIAL SYSTEM AND THE SPREAD OF CANCER, ESPECIALLY OF GASTRIC CARCINOMA. (E.) Omori, Y. (Dept. Surg., Niigata U. Sch. Med., Japan). Tohoku J. Exp. Med. 81(4):315-321, 1964.

Among 139 pts. with gastric carcinoma, 80% showed a positive association between RES hypofunction (as measured by the Congo Red Index) and poor postoperative diagnosis. In these pts., the degree of dissemination of the cancer was directly proportional to the degree of reduction of RES activity. No evidence of RES hypofunction was seen in 40% of a subgroup in which the gastric cancer was specifically localized, without metastasis. No metastases were seen in 51% of the pts. who showed a high degree of sinus histiocytosis (SH) of the regional lymph nodes as compared to only 19% of those who showed reduced or absent SH. RES activity in the stromal tissue adjacent to the primary lesion was reduced in cases with a high degree of dissemination and short survival times, but was markedly increased (as was SH) in cases surviving more than 5 yr. after surgery. The author concludes that a definite relationship exists between tumor spread and RES activity.

64-1593 EOSINOPHILIC GRANULOMA WITH TRANSITION TO RETICULUM CELL SARCOMA AND

EOSINOPHILIC GRANULOMA OF AN ATYPICAL PRIMARY SITE. (E.) Christoffersen, P. (Glostrup Hosp., Denmark) and A. R. Nielsen. Acta Path. Microbiol. Scand. 60(3):334-342, 1964.

In a 35-year-old woman with a destructive process involving the neck of the humerus, a biopsy specimen was diagnosed histologically as eosinophilic granuloma. Six mo. later, with 2 courses of local X-ray intervening, both a 2nd biopsy specimen and an operative specimen were diagnosed histologically as reticulum cell sarcoma. A second case is presented of a 3-year-old girl with a bone lesion which was diagnosed as eosinophilic granuloma and clinically represented a transition between this condition and Letterer-Siwe's disease.

64-1594 PRIMARY CARCINOMA OF BILE DUCT OF THE LIVER OF THE CAT (*FELIS CATUS*) INFESTED WITH *CLONORCHIS SINENSIS*. (E.) Hou, P. C. (Chinese Med. Coll., Peking). J. Path. Bact. 17(2):239-244, 1964.

Among 215 cats obtained at random were 2 females with primary carcinomas of the secondary hepatic bile ducts. The livers of these cats were infested with *Clonorchis sinensis*. After feeding of fish containing clonorchis cysts to 26 cats, a primary hepatic carcinoma of the same sort was found in 1 cat that died of pneumonia 130 days after start of diet. The author concludes that *C. sinensis* is directly responsible for inducing all 3 cancers, possibly, as a result of mechanical and/or chemical irritation of the adenomatous tissue lining the affected bile ducts. All these cats were about 4 yr. of age and hence represent "middle age". It is noted that this cancer in the same site and caused by *C. sinensis* is now recorded for 3 vertebrates: man, dog and cat.

64-1595 PARABIOTIC CELL CULTURE. IV. INTERACTION BETWEEN NORMAL AND ASCITES TUMOR CELLS OF RATS. (E.) Katsuta, H. (Inst. Infect. Dis., U. Tokyo, Japan) and T. Takaoka. J. Nat. Cancer Inst. 32(5):963-980, 1964.

Using the parabiotic cell culture method, interaction between the cells from normal tissue (liver cells, heart fibroblasts and kidney epithelial cells) and transplantable ascites tumor cells (hepatoma AH-130 and Yoshida sarcoma) of rats was examined quantitatively by cell counting. In single cultures or cultures in matched tubes of liver and hepatoma cells, or of fibroblast and sarcoma cells, the proliferation of tumor cells was apparently accelerated in the parabiotic culture, while normal cells were inhibited or destroyed. The possibility of direct action by cell contact is suggested by the fact that the above phenomenon was further accelerated by cultivation of cells together in a single tube. In other combinations between these normal and tumor cells, little interaction was observed.

64-1596 CHROMOSOMAL ABNORMALITY AND CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Fitzgerald, P. H. (Christchurch Hosp., New Zealand) and F. W. Gunz. Lancet 2:150, 1964.

The author reports making chromosomal examinations in 4 families with more than 1 case of chronic lymphatic leukemia (CLL). In 2/4, 1 sibling had the disease and a 2nd had died of it previously; in 1/4, 2 siblings had the disease and a 3rd had died previously of chronic granulocytic leukemia; in 1/4, 1 sibling had the disease and another had died of leukemia previously, probably of the granulocytic type. There was no trace of an inherited chromosome abnormality (Ch¹) or of any similar congenital abnormality in any of the living pts. or in an unspecified number of non-leukemic relatives who were also examined. These pts. brought the total of CLL pts. examined to date to 30. The author concludes that inherited chromosomal abnormalities of a visible size are not of general significance as factors predisposing to chronic lymphatic leukemia, although this does not lessen the possibility that the Ch¹ abnormality, when present, may predispose its carrier to the disease. (See also CRA 2(4):#798, 1964.)

64-1597 THE PROBLEM OF "SEX CHROMATIN" IN TUMORS. (Ger.) Regele, H. (Inst. Path.-Anat., U. Wien, Germany), F. Kaufmann and H. Wasl. Krebsarzt 19(1):11-17, 1964.

Designating a rate of 18-20% or more of nuclei with sex chromatin (Barr's bodies) as positive, the distribution in 510 cases of mammary carcinoma was 287 positive and 223 negative. The positive cases were most frequent in the age group 60 and over. Histopathological differences and presence or absence of metastases did not seem to affect the ratio of positive to negative cases. In an analysis of survival and type of therapy in breast cancer, it was found that androgen therapy was favorable in sex chromatin positive cases but not in negative ones.

64-1598 CONGENITAL LEUKAEMIA. (E.) Sobti, P. (Dept. Med., Irwin Hosp., New Delhi, India). J. Indian Med. Assn. 43(4):179-181, 1964.

A case of congenital leukemia in a newborn boy is presented; the mother had received no X-irradiation before or during pregnancy. The past histories of the parents and their families were of no significance.

64-1599 A STUDY OF CHROMOSOMES IN CHRONIC GRANULOCYTIC LEUKEMIA. (Rum.) Nicolau, C. T. (Rumanian Acad. Sci., Bucharest), E. R. Popescu, S. T. Nicoară, B. Wechsler, E. Butoianu and S. Taigăr. Med. Intern. (Bucur.) 16(7):775-782, 1964.

Direct cytogenetic examination was made of the

sternal or iliac bone marrow of 10 pts. (5 men, 5 women; age 37-67 yr.) with chronic granulocytic leukemia. Adequate preparations were obtained for 6 of the pts., all of which showed the Philadelphia chromosome; in 2 previously treated with busulfan there was also present a small chromosome of the D group (13-15).

64-1600 BASAL CELL EPITHELIOMA: ITS LOCALIZATION ALONG THE LINES OF THE EMBRYONAL FACIAL CLEFT. (Jap.) Miki, Y. (Dept. Derm., Osaka U. Sch. Med., Japan). Hifu To Hinyo (Derm. Urol. [Fukuoka]) 18(4):331-335, 1964.

See CRA 2(5):#1010, 1964.

64-1601 CONGENITAL LEUKEMIC RETICULOSIS (MYELO-RETICULOSIS) IN A PREMATURE INFANT. (Ger.) Škodáček, G. (Child. Dept., City Hosp., Komarno, Czech.) and J. Babala. Neoplasma (Bratisl.) 11(2):199-206, 1964.

A premature female infant born with generalized infiltrations of leukemic reticulosis (myeloreticulosis) died in 5 days despite treatment. Family history revealed that the father was occupationally exposed to X-rays, while repairing X-ray apparatus.

64-1602 STUDIES OF THE BEHAVIOR OF TUMOR TISSUES IN DIFFUSION CHAMBERS IN THE PRESENCE OF PENETRATING HOST CELLS IN TUMOR-RESISTANT RATS. (Ger.) Teichmann, B. (Robert-Rossle Hosp., German Acad. Sci. Berlin). Experientia 20(6):327-328, 1964.

Supplementing previous studies on the behavior of tumor cells in diffusion chambers implanted in Wistar rats (see CRA 2(3):#449 and #569, 1964; and *ibid.*, 2(7):#1401, 1964), the author now reports evidence that the destruction of Walker carcinoma and Jensen sarcoma tumor cells in such implanted diffusion chambers can result from immunologic processes only when sensitized (immunized) cells from the host animal penetrate the chambers through membrane filters of relatively large pore size. The degree of destruction was directly proportional to the number of sensitized cells (lymphocytes measuring 7-9 μ) which pene-

trated the chamber. When the pore size of membrane filters prevented or considerably impeded penetration of lymphocytes, tumor cells in the chambers remained viable and capable of inducing tumors when inoc. subsequently into experimental animals.

64-1603 PAPILLARY CYSTADENOFIBROMA OF THE OVARY WITH MALIGNANT TRANSFORMATION AND METASTASES. REPORT OF A CASE AND REVIEW OF THE LITERATURE. (E.) Coyle, W. R., III (Dept. Obstet. Gynec., St. Vincent's Hosp., New York, N. Y.) and R. Gettinger. Obstet. Gynec. 23(4):593-597, 1964.

A case is described of a metastasizing adenocarcinoma in a 30-year-old Cuban woman, which developed from the epithelium of an ovarian cystadenofibroma. This is the second case reported of such a malignant transformation, and the first to show metastasis. Theories of its pathogenesis are presented, and the pertinent literature is reviewed (11 references).

64-1604 EFFECT OF PARENTERAL HETEROLOGOUS ALBUMIN ON TRANSPLANTED TUMORS IN MICE. (E.) Gazet, J.-C. (Dept. Surg., U. Illinois Coll. Med., Chicago) and B. McKibbin. Proc. Soc. Exp. Biol. Med. 115(3):740-744, 1964.

In female Swiss mice (age 4-6 wk.; wt. approx. 20 g) inoc. with Sarcoma 180 or Ehrlich ascites tumor cells, the s.c. admin. of bovine albumin (125 mg/kg/day or 2 g/kg in 14 days) increased tumor incidence from 59%-92% and from 54%-91%, resp., as compared to animals given saline. Similar, but less significant, results were obtained with albumin hydrolysate. Since prior incub. *in vitro* of albumin with these tumor cells did not enhance the effect, it is suggested that albumin does not act directly upon the tumor cell.

64-1605 EMBRYONAL SERUM ALPHA-GLOBULIN AND ITS SYNTHESIS BY TRANSPLANTABLE MOUSE HEPATOMAS. (Rus.) Abelev, G. I., S. D. Perova and N. I. Khramkova. Biokhimiia 28:625-634, 1963.

See CRA 2(3):#579, 1964.

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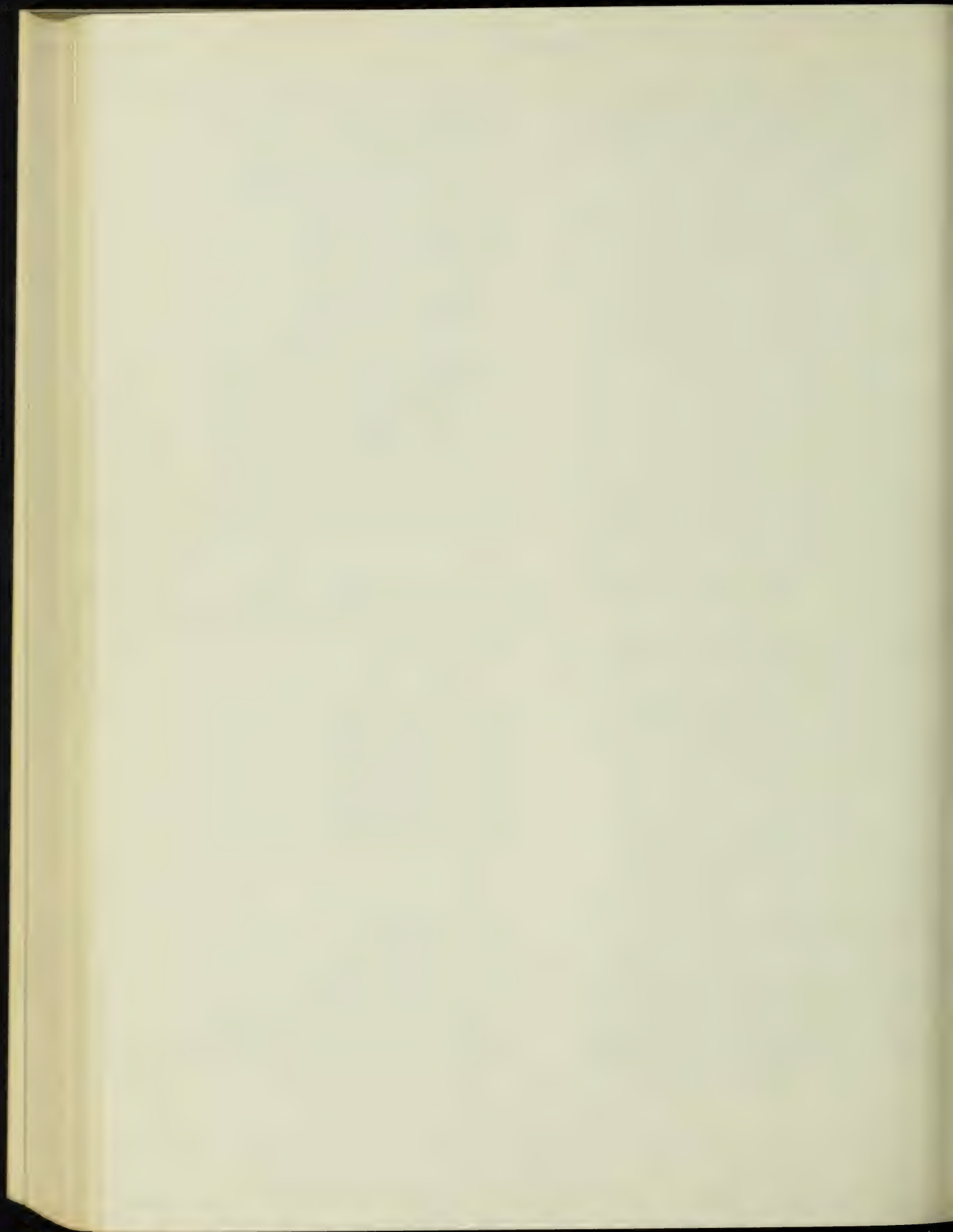
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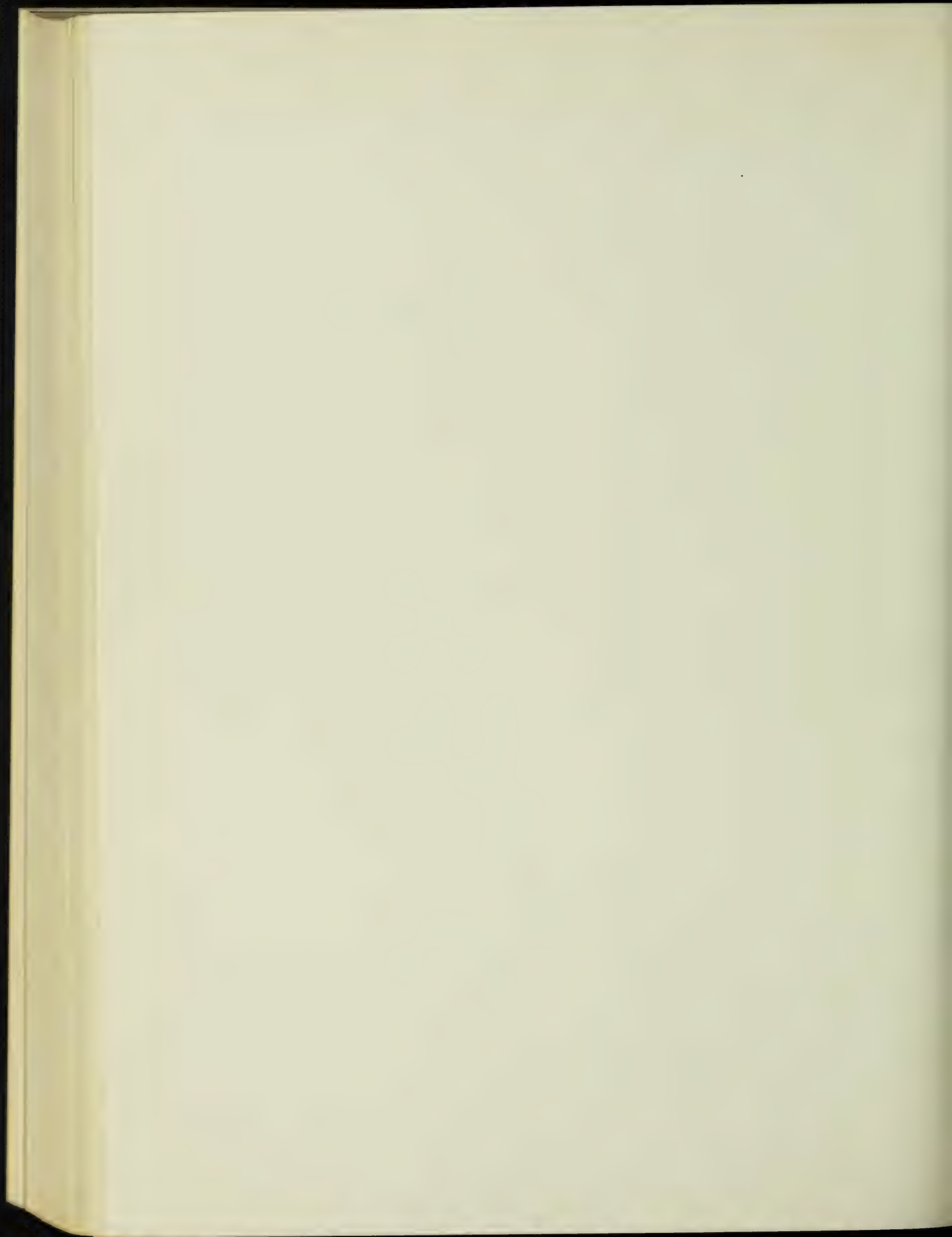
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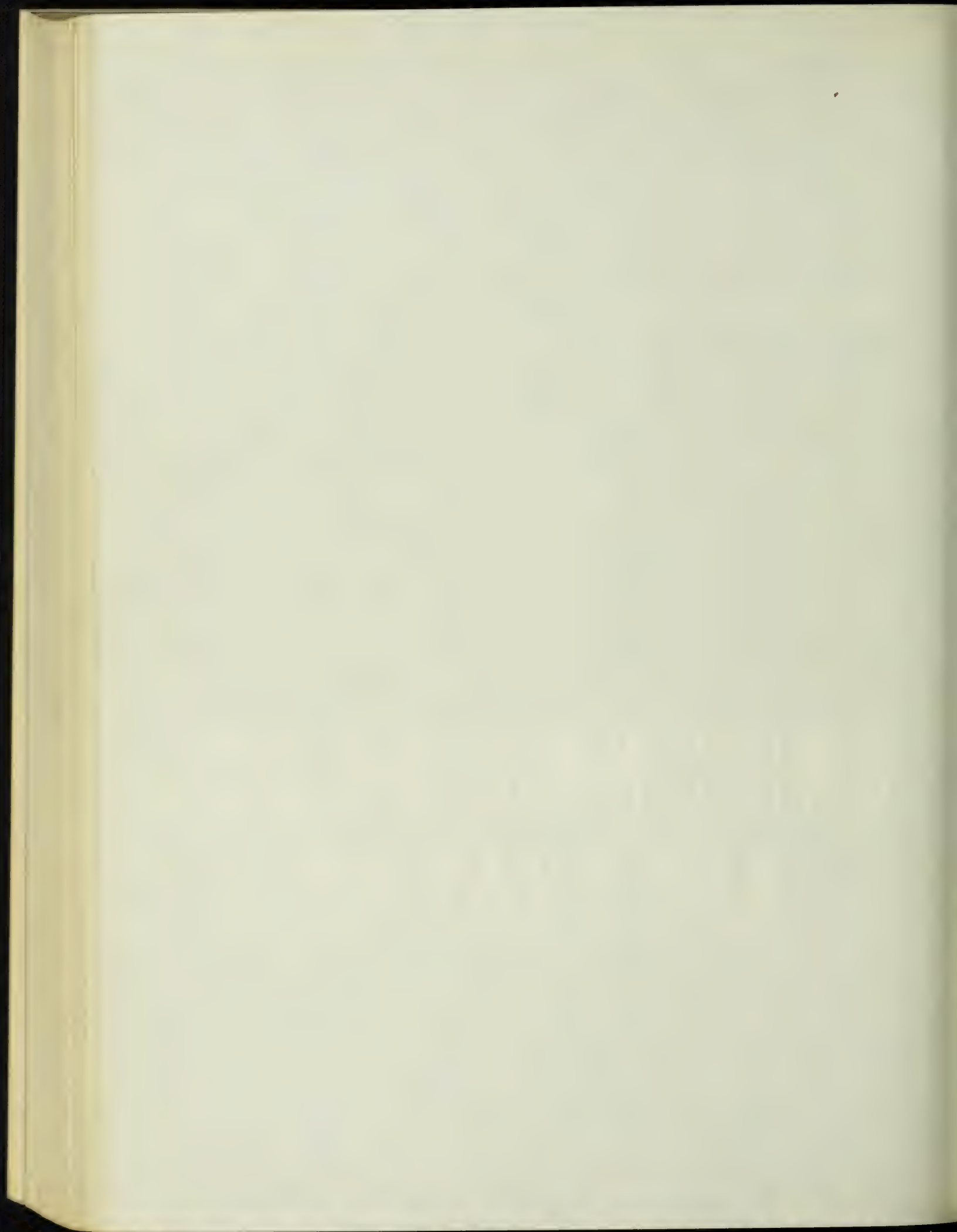
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National Cancer Institute

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FOREWORD

The National Cancer Institute, in response to Congressional interest and desire for a national program of cooperative research in cancer, is establishing a means whereby information in the field of carcinogenesis will be coordinated and made available. The information to be included will be obtained from the National Cancer Institute, other governmental agencies, and non-governmental research institutions.

The issuing of Carcinogenesis Abstracts under the auspices of the National Cancer Institute will provide a central source for current abstracting of the carcinogenesis literature being published throughout the world. This will help facilitate an integrated and cooperative program of investigation in this area. The growing number of publications in the area of carcinogenesis makes imperative the availability of an appropriate abstracting service so that investigators may be apprised of progress with a minimum of delay. It is our desire to provide the investigator with a readily systematized compilation of the published work.

Carcinogenesis Abstracts will be published monthly and will include abstracts from journals received primarily the month previously.

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